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Acute Intravenous Toxicity Study of Hypertonic Saline/Dextran 70® and its Constituents in New Zealand White Rabbits

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DIVISION OF TOXICOLOGY

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Acute Intravenous Toxicity Study of Hypertonic Saline/Dextran 70® and its Constituents in New Zealand White Rabbits (Toxicology Series 246) --Zaucha *et al*

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19 ABSTRACT (Continue on reverse if necessary and identify by block number)

[illegible] following intravenous administration of a [illegible], hypertonic saline/Dextran 70® (HSD), was evaluated [illegible] New Zealand White rabbits. Animals received a single [illegible] 10 ml/kg over a 5-minute period, in an attempt [illegible] dosage. Equal volumes of each HSD component, 7.5 [illegible] (HS) and 6% Dextran 70® (D70) in normal saline, and Ringer's [illegible] were also evaluated. The animals in each group were divided [illegible] necropsy, either Day 3 or Day 14 after dosing [illegible] for serum chemistry and hematologic analyses [illegible] Observations were made at 1, 2, and [illegible] the day [illegible] and twice daily thereafter. HS [illegible] at the start of injection in 6 of 20 rabbits [illegible] the HS and HSD groups exhibit[illegible]

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19. SPECIFIC TERMS (cont.)

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20. ABSTRACT (cont.)

Increased incidence of bruising of the injected ear, inactivity, disorientation, and tremors. Compared to the controls, all groups exhibited increased respiratory rate. Except for decreased serum iron in the HS group 5 days after administration, no consistent changes were seen in serum chemistry measurements. No significant changes outside of normal limits were observed in the hematology measurements. Body weights and water consumption were unaffected by the dosing and no gross or microscopic lesions could be attributed to HSD or its constituents. These data suggest that the lethality of HS was due to an acute hemodynamic effect of the volume administered, and that the rabbit was less sensitive to HSD or D70 than to HS. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate minimal adverse effects should be anticipated with the therapeutic administration of HSD.

ABSTRACT

The acute toxicity following intravenous administration of a proposed resuscitation fluid, hypertonic saline/ Dextran 70® (HSD), was evaluated in male and female New Zealand White rabbits. Animals received a single intravenous dose of HSD, [illegible] ml/kg over a 5-minute period, in an attempt to define maximum tolerated dosage. Equal volumes of each HSD component, 7.5% hypertonic saline (HS) and 6% Dextran 70® [illegible] in normal saline, and Ringer's lactate (RL) were also evaluated. The animals in each group were divided into two subgroups according to necropsy, either Day 3 or Day 14 after dosing. Blood samples were collected for serum chemistry and hematologic analyses at necropsy on Day 3, and on Day 13. Observations were made at 1, 2, and 4 hours after administration on the day of dosing and twice daily thereafter. HS produced death within 12 minutes of the start of injection in 6 of 20 rabbits. Compared to the control animals receiving RL, the HS and HSD groups exhibited increased incidence of bruising of the injected ear, inactivity, disorientation, and tremors. Compared to the controls, all groups exhibited increased respiratory rate. Except for decreased serum iron in the HS group 3 days after administration, no consistent changes were seen in serum chemistry measurements. No significant changes outside of normal limits were observed in the hematology measurements. Body weights and water consumption were unaffected by the dosing and no gross or microscopic lesions could be attributed to HSD or its constituents. These data suggest that the lethality of HS was due to an acute hemodynamic [illegible] of the volume administered, and that the rabbit was [illegible] sensitive to HSD or D70 than to HS. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings [illegible] minimal adverse effects should be anticipated with [illegible] therapeutic administration of HSD.

Keywords: Acute Toxicity, Intravenous Injection, Maximum Tolerated Dose, Hypertonic Saline/Dextran 70®, Hypertonic Saline, Dextran 70®, Ringer's Lactate, Resuscitation Fluid, New Zealand White Rabbits

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PREFACE

TYPE REPORT: Acute Toxicity GLP Study Report

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Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800

SPONSOR: US Army Medical Research and Development Command
Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800
Project Director: Charles Wade, PhD

PROJECT/WORK UNIT/APC: 3S463807D836/087/TLRO

GLP STUDY NUMBER: 88002

STUDY DIRECTOR: Don W. Korte, Jr., PhD, LTC, MSC
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PRINCIPAL INVESTIGATOR: Gary M. Zaucha, DVM, CPT, VC

CO-PRINCIPAL INVESTIGATOR: Denzil F. Frost, MS, DVM, CPT, VC
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PATHOLOGIST: Luann McKinney, DVM, MAJ, VC
Diplomate, American College of
Veterinary Pathologists

DATA MANAGER: Yvonne C. LeTellier, BS

REPORT AND DATA MANAGEMENT: A copy of the final report, study protocols, retired SOPs, raw data, analytical and stability data, and an aliquot of the test compound will be retained in the LAIR Archives.

TEST SUBSTANCE: Hypertonic Saline/Dextran 70®

INCLUSIVE STUDY DATES: 24 August 88 - 4 October 88

OBJECTIVE: The objective of this study was to determine the acute toxicity of hypertonic saline/Dextran 70® following intravenous administration in male and female New Zealand White rabbits.

ACKNOWLEDGMENTS

SPC Dean K. Magnuson, BS, SPC Eric Dahlberg, BS, and SPC Vilmar O. L. Villa provided assistance in dose preparation and administration; SGT Tammie Heineman, SGT Barbara D. Green, and Richard Katona provided data collection, animal care, and facility management.

SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS INVOLVED IN THE STUDY

We, the undersigned, declare that GLP study number 88002 was performed under our supervision, according to the procedures described herein, and that this report is an accurate record of the results obtained.

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DEPARTMENT OF THE ARMY

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REPLY TO
ATTENTION OF:

SGRD-ULZ-QA

28 March 1988

MEMORANDUM FOR RECORD

SUBJECT: GLP Compliance for GLP Study 88002

1. This is to certify that in relation to LAIR GLP Study 88002, the following inspections were made:

27 January 1988	-	Protocol Review
17 June 1988	-	Animal Receipt/Room Inspection
06 July 1988	-	Randomization
11 July 1988	-	Dosing
25 July 1988	-	Necropsy
25 July 1988	-	Test Chemical Log
25 August 1988	-	Animal Receipt
12 September 1988	-	Randomization
13 September 1988	-	Dosing
13 September 1988	-	Observations/Scoring
16 September 1988	-	Interim Sacrifice
26 September 1988	-	Weighing Water Bottles
27 September 1988	-	Necropsy
27 September 1988	-	Serum Chemistry Check

2. The institute report entitled "Hypertonic Saline/Dextran 70® and its Constituents in New Zealand White Rabbits," Toxicology Series 246, was audited on 24 February 1989.

Walter G. Bell
WALTER G. BELL
SFC, USA
Quality Assurance Auditor

TABLE OF CONTENTS

Page

Abstract.....i

Preface.....iii

Acknowledgments.....iv

Signatures of Principal Scientists.....v

Report of Quality Assurance Unit.....vi

Table of Contents.....vii

BODY OF REPORT

INTRODUCTION.....1

Objective of Study.....2

MATERIALS.....2

Test Substance.....2
Test Substance Constituents.....2
Control.....3
Animal Data.....3
Husbandry.....3

METHODS.....4

Group Assignment/Acclimation.....4
Dose Levels, Preparation, and Analysis.....5
Test Procedures.....5
Observations.....5
Necropsy.....6
Statistical Analysis.....6
Duration of Study.....6
Changes/Deviations.....6
Storage of Raw Data and Final Report.....7

RESULTS.....7

Clinical Observations.....7
Body Weights.....8
Water Consumption.....8
Serum Chemistry.....9
Hematology.....9
Necropsy Findings.....9

TABLE OF CONTENTS (continued)

Page

DISCUSSION.....10

CONCLUSION.....28

REFERENCES.....29

APPENDICES.....31

Appendix A. Chemical Data.....32
Appendix B. Animal Data.....36
Appendix C. Historical Listing of Events.....37
Appendix D. Individual Animal Histories.....38
Appendix E. Body Weights.....66
Appendix F. Water Consumption.....70
Appendix G. Serum Chemistry.....74
Appendix H. Hematology.....87
Appendix I. Pathology Report.....96

OFFICIAL LIST OF DISTRIBUTION.....186

Acute Intravenous Toxicity Study of Hypertonic Saline/Dextran 70® and Its Constituents in New Zealand White Rabbits -- Zaucha *et al*

INTRODUCTION

During conventional land warfare it has been estimated that 90% of the deaths occur either in the field or en route to a fixed medical treatment facility and that 50% of those deaths occur due to hemorrhage (1). Conventional treatment of hemorrhage has involved infusion of isotonic resuscitation fluids at volumes equivalent to two or three times the volume of blood lost (2). Supplying this volume of resuscitation fluid on the battlefield for treatment of multiple casualties is not feasible.

Hypertonic crystalloid solutions have been used for the past 70 years in the treatment of hemorrhage (3). However, the consensus has been that unless followed by replacement of the lost blood volume, the beneficial effects of treatment with hyperosmotic solutions are transient (4). Recently, the addition of a hyperoncotic colloid, 6% Dextran 70®, to the hypertonic crystalloid, 7.5% saline, has significantly extended 96-hour survival rates compared with those obtained with normal saline or 7.5% saline (5). Should the effectiveness of this hypertonic saline/Dextran therapy be verified by clinical trial, it would provide a significant advance in the treatment of blood loss due to traumatic injuries.

As with any new treatment regimen, there are potential risks. Low molecular weight dextran could cause bleeding abnormalities and phlebitis or possibly interfere with the cross-matching of blood (6). Hypertonic solutions could cause neurologic abnormalities induced by the rapid increases in osmolalities (7-9) or cardiac arrhythmias induced by the hypokalemia associated with the rapid expansion of extracellular space (2, 10). Consequently, the Division of Toxicology, Letterman Army Institute of Research, was tasked to provide an acute and subchronic toxicity profile of the 7.5% hypertonic saline/6% Dextran 70® resuscitation fluid (HSD). This report describes the results of an acute toxicity study of hypertonic saline/Dextran 70® following intravenous administration of the maximum tolerated dose in male and female New Zealand White rabbits.

Objective of Study

The objective of this study was to determine the acute toxicity of hypertonic saline/Dextran 70® following intravenous administration in male and female New Zealand White rabbits.

MATERIALS

Test Substance

Name: Hypertonic saline/Dextran 70® (HSD)

LAIR Compound Code: TP96

Lot Number: NC 54845

Expiration Date: September 1989

Composition per 100 ml:

Dextran 70®	6 g
sodium chloride	7.5 g
water for injection to 100 ml	

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Test Substance Constituents

Name: Hypertonic (7.5%) saline (HS)

LAIR Compound Code: TP98

Lot Number: I 318712

Expiration Date: 31 December 1988

Composition per 100 ml:

sodium chloride	7.5 g
water for injection to 100 ml	

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Name: Dextran 70® (D70)

LAIR Compound Code: TP95

Lot Number: NE 54941

Expiration Date: 31 May 1989

Composition per 100 ml:	Dextran 70®	6 g
	sodium chloride	0.9 g
	water for injection to 100 ml	

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Control

Name: Ringer's lactate (RL)

LAIR Compound Code: TP97

Lot Number: NC 54847

Expiration Date: September 1989

Composition per 100 ml:	sodium chloride	600 mg
	potassium chloride	30 mg
	calcium chloride dihydrate	20 mg
	sodium lactate	310 mg
	water for injection to 100 ml	

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Other test substance information is presented in Appendix A.

Animal Data

Forty male and 40 female New Zealand White rabbits (Hazleton Research Products, Inc., Swampbridge Rd., Denver, PA 17517) were assigned to this study. They were identified individually with ear tags. The animal weights on receipt (24 August 88) ranged from 2.447 to 3.732 kg. Additional animal data are presented in Appendix B.

Husbandry

Study animals were individually housed in stainless steel battery-type cages with screen bottoms, in racks equipped with automatically flushing dump tanks. The diet, fed *ad libitum*, consisted of Certified Purina Rabbit Chow® 5322 (Ralston Purina Company, St. Louis, MO); water, purified by reverse osmosis, was provided by individual water bottles with sipper tubes. The animal room temperature and humidity were monitored continuously by hygrothermograph. The

temperature was maintained in a range from 17.2°C to 23.3°C. The relative humidity was maintained in a range of 27% to 65% with occasional spikes to as high as 90% during room cleaning. The photoperiod was 12 hours of light per day (0600 - 1800 hours).

METHODS

This study was conducted in accordance with FDA guidelines (11) and LAIR SOP-OP-STX-113, "Acute Intravenous Toxicity Study" (12).

Group Assignment/Acclimation

The animals were randomized into four groups of 10 male and 10 female animals each. Since animals were to be terminated at two different time intervals following dosing, the first 5 male and 5 female animals of each group were designated for interim sacrifice (Day 3) with the remainder designated for terminal sacrifice (Day 14) (Table 1). Allocation was accomplished using a computer-based, stratified, weight-biased method. The XYBION Path/Tox AESLCT Animal Allocation Program was used in conjunction with a VAX 750 Computer.

Table 1

DOSE GROUPS

Group	n (each sex)	Solution	Sacrifice Day
1	5	hypertonic saline	3
1	5	hypertonic saline	14
2	5	hypertonic saline/Dextran 70®	3
2	5	hypertonic saline/Dextran 70®	14
3	5	Dextran 70/normal saline	3
3	5	Dextran 70/normal saline	14
4	5	Ringer's lactate	3
4	5	Ringer's lactate	14

The male and female study animals were acclimated for 19 and 26 days, respectively, before the day of dosing. During this period they were checked daily for signs of illness, and weighed weekly.

Dose Levels, Preparation, and Analysis

The maximum tolerated intravenous dose of HSD administered over a 5-minute period was determined to be 20 ml/kg in preliminary pilot studies. Equal volumes of HS, D70, and RL were administered to animals in the corresponding dose groups. Solutions were used as supplied by the manufacturer, Pharmacia LEO Pharmaceuticals. Analysis of the dosing solutions was provided by Pharmacia LEO Pharmaceuticals. Additional chemical data are presented in Appendix A.

Test Procedures

The acute intravenous toxicity of hypertonic saline/Dextran 70® (HSD) was evaluated in parallel with solutions of its major constituents, hypertonic (7.5%) saline (HS) and Dextran 70® (6%) in normal saline (D70), with Ringer's lactate (RL) serving as the control. The dosing solutions were administered via the marginal ear veins. Injections were made using 60 cc syringes (Becton Dickinson & Co., Rutherford, NJ 07070, Lot No. 5M516) and 23-gauge, 1-inch needles (Becton Dickinson & Co., Rutherford, NJ 07070, Lot No. 7F018). A 12-inch length of PE-50 polyethylene tubing (Clay Adams, Division of Becton Dickinson & Co., Parsippany, NJ 07054, Lot No. 93590, exp. date 3/93) was used to attach a second, hubless needle to the needle on the syringe to facilitate completion of the injections. Immediately following the injection, digital pressure was applied to control any bleeding from the injection site.

Observations

Clinical observations were accomplished 1, 2, and 4 hours after dosing on Day 0, and then at least twice daily for the remainder of the observation period. Body weights were recorded upon receipt of the animals, weekly during the quarantine and observation periods, before dosing, and at necropsy. Water consumption was monitored for a twenty-four hour period, weekly during quarantine, daily for the first week of the study, and at 14 days. Blood was collected for serum chemistry and hematology analyses at necropsy on Day 3 and on Day 13. All samples for serum chemistry and clotting

time determinations were centrifuged after collection and the serum or plasma frozen for a week before being analyzed.

Necropsy

Animals that died spontaneously after dosing were immediately submitted for necropsy. Interim and terminal sacrifice animals were submitted for necropsy on Days 3 and 14, respectively, immediately after sacrifice by barbiturate overdose. Histopathologic examination was performed on the heart, liver, kidney, brain, lung, spleen, and all gross lesions.

Statistical Analysis

Clinical signs were tabulated by groups. The means and standard deviations for the body weights, water consumption, serum chemistry, and hematology data for each group were calculated. For the body weights, serum chemistry, and hematology data, an analysis of variance and the Bartlett's test for homogeneity were performed using the XYBION PATH/TOX software package. If the F-statistic was significant for an analysis of variance for a particular measurement, differences from the control were evaluated using the Dunnett's test for homogeneous data and the Modified T test for nonhomogeneous data. Using the BMDP statistical software package, the equality of the variances for the groups' water consumption was tested by the Levene test. If equal, the standard one-way analysis of variance was performed. If unequal, the Welch's one-way analysis of variance was performed. If the F-statistic was significant for an analysis of variance for a particular measurement, differences among the groups were evaluated using the Newman-Keuls test (13). For total bilirubin, the Kruskal-Wallis nonparametric one-way analysis of variance was performed (13). Gross and microscopic pathology findings were described for each animal and tabulated by groups.

Duration of Study

Appendix C is a complete listing of historical events.

Changes/Deviations

Water consumption was not recorded on Day 7 and Day 14 for the males and females, respectively. Body weights were not recorded for the females on Day 7. Terminal sacrifice blood samples were taken from the central artery of the ear on Day 13 instead of Day 14 to avoid hemolysis induced by pentobarbital anesthesia at euthanasia and necropsy. The

prothrombin time and activated partial thromboplastin time data are designated as "NT" when hemolysis and clumping of the samples interfered with the test procedure. Hematology data are unavailable for animals 88F00-301, 308, 324, 336, 338, and 344 due to clotting or lack of sufficient sample obtained at interim sacrifice. The protocol schedule refers to the day of dosing as Day 0. Since XYBION programming refers to the day of dosing as Day 1, a one-day discrepancy exists between the actual study day and the day listed in the XYBION printouts for Serum Chemistry, Hematology, and Pathology appendices. Day 4, 14, and 15 listed in each of these appendices refers to study days 3, 13, and 14, respectively. In an attempt to equalize the number of animals scheduled for Interim Sacrifice and Terminal Sacrifice, animal # 310, originally scheduled for Terminal Sacrifice, was moved up into the Interim Sacrifice group. The need to reschedule was due to 3 deaths in the HS Interim Sacrifice group.

It is believed that these changes had no adverse effects on the results of this study.

Storage of Raw Data and Final Report

A copy of the final report, study protocol, raw data, retired SOPs, and an aliquot of the test compound will be retained in the Letterman Army Institute of Research Archives.

RESULTS

Clinical Observations

The clinical signs observed were grouped into the following categories: behavioral, respiratory, injection site reactions, death, ocular, reflexive, food consumption, and gastrointestinal.

The category of signs most frequently observed was behavioral. Inactivity (27 of 80 animals) was observed throughout the study period in males and females, but was most frequently seen on Day 0 (14 animals) following dosing. In the males, inactivity was seen with equal distribution among dose groups. However, in the female animals, the HSD and HS groups were primarily affected (7 and 6 animals, respectively). Disorientation (22 of 80) was observed on Day 1 in both sexes with greatest incidence in the females. Disorientation was observed most frequently in the HS (10 animals) and HSD (8 animals) groups. Tremors (12 of 80) were

also observed primarily in the HS and HSD groups and only on Day 0. Males and females were affected equally with tremors. Infrequently observed behavioral signs included aggression (4 of 80), hyperactivity (3 of 80), and irritability (1 of 80). These signs were sporadically observed among the different dose groups.

The second major category of clinical signs observed in the study was respiratory signs. Increased respiratory rate was observed in 33 of 80 animals on Day 0. Respiratory rate returned to normal in all affected animals by Day 1. The increase in respiratory rate occurred primarily in female animals receiving HSD, HS, or D70.

Bruising of the injected ear was observed in 12 animals (8 males and 4 females) from the HSD- and HS-treated groups. Fluid or bloody discharge, discoloration, and necrosis of the injection site also occurred in several HSD and HS animals.

Six animals receiving HS (3 males and 3 females) died within 12 minutes of the start of the infusion. No other mortalities were observed during the study period.

Ocular signs were observed in 2 of 80 animals. Both animals were HS-treated males. The eyes of these animals became pale or a lighter red in color. The pale eyes were first observed on Day 0 with the condition persisting for 1 and 3 days in each respective animal.

Other signs were isolated in nature and occurred sporadically among the different groups. Increased startle reflex (reflexive), diarrhea (gastrointestinal), and decreased appetite (food consumption) were observed in one animal each.

A summary of clinical observations is presented in Table 2. Individual animal histories are presented in Appendix D.

Body Weights

Animal body weights were not significantly ($p \leq 0.05$) affected by dosing. Group mean body weights are presented in Table 3. Individual animal body weights are presented in Appendix E.

Water Consumption

Water consumption was not significantly ($p \leq 0.05$) affected by dosing. Group mean water consumption data are

presented in Table 4. Individual animal water consumption data are presented in Appendix F.

Serum Chemistry

Group mean serum chemistry data are presented in Table 5. Individual serum chemistry data are presented in Appendix G. At interim sacrifice, the mean iron of the male HS group was significantly less than that of the controls ($p = 0.01$), with all 3 interim sacrifice HS males having abnormally low values (14). The mean iron of the female HS group was also reduced at interim sacrifice, but the difference from the controls was not statistically significant ($p \leq 0.05$). The mean triglyceride values of the male HSD, HS, and D70 groups were significantly greater than that of the controls ($p = 0.05$) at interim sacrifice, but the values were within accepted normal limits (15). The magnesium of the female HS group was significantly less than that of the controls at interim sacrifice ($p = 0.05$), but the value was within normal limits (14). At terminal sacrifice, the male HSD and HS groups had mean alanine amino-transferase levels significantly less than that of the controls ($p = 0.01$ and 0.05, respectively), but the values were within normal limits (14). The serum chemistries of the female dose groups were not significantly different from those of the controls at terminal sacrifice.

Hematology

Group mean hematology data are presented in Table 6. Individual hematology data are presented in Appendix H. Hematology parameters of the females study animals at interim sacrifice were not significantly affected by dosing ($p \leq 0.05$). At interim sacrifice, the male animals receiving HS had a mean erythrocyte count significantly less than that of the controls ($p = 0.05$), but the value was within normal limits (16). At terminal sacrifice, the male HSD group had a mean reticulocyte count significantly less than that of the control group ($p = 0.05$), but this value was also within normal limits (16). The mean prothrombin times of the female HSD and D70 groups were significantly greater than that of the control group at terminal sacrifice ($p = 0.05$), but the values remained within acceptable limits.

Necropsy Findings

No gross or microscopic pathological lesions attributable to the test compound or its constituents were reported. The Veterinary Pathologist's report is presented in Appendix I.

DISCUSSION

The acute intravenous toxicity of HSD in rabbits was evaluated by dosing the animals with an apparent maximum tolerated dose via the marginal ear vein. This dose was established in preliminary studies as 20 ml/kg administered over 5 minutes. This dose, 20 ml/kg, is five times the proposed therapeutic dose of 4 ml/kg (2). In addition to dosing with HSD, groups of rabbits were dosed with equal volumes of HS, D70, or RL. No mortalities were observed when HSD was administered at a rate of 20 ml/kg over 5 minutes. However, the HS caused death in 3 of 10 males and 3 of 10 females dosed, suggesting that the HS component has greater toxicity than the HSD mixture, and the maximum tolerated dose is less than 20 ml/kg for the HS component alone. The deaths were very rapid, occurring within 3 - 12 minutes of the initiation of the infusion. Since death occurred rapidly and only in the group receiving hypertonic saline, the deaths could be attributed to cardiac dysrhythmia arising from the putative hypokalemia produced by the saline infusion. This is consistent with the observation that dextran is well tolerated when administered intravenously at doses up to 40 ml/kg in various animal models (G. Jonsson, Pharmacia Pharmaceuticals AB, personal communication).

An equal volume of RL was administered as a control. Since the RL is an isotonic solution, it would only permit comparison of the effects of the volume administered. Therefore, differences between the RL group and the HSD, HS, and D70 groups can be attributed to the volume expansion capabilities of the latter groups.

Inactivity, disorientation, tremors, increased respiratory rate, bruising of the injection site, and pale eyes were observed at an increased rate in the HS and HSD-treated groups. The D70-treated animals also exhibited a greater incidence of increased respiratory rate when compared to the controls.

The increased incidence of behavioral signs appeared to be limited to animals receiving HS-containing solutions, which again suggests that the toxicity of HSD is due to the HS component, although behavorial signs were also noted in the female D70 group.

Table 2

CLINICAL OBSERVATIONS SUMMARY*

Group (n) Observation	RL (10)	HSD (10)	HS (10)	D70 (10)
	Males			
NORMAL/NO SIGNIFICANT SIGNS	7	3	0	7
BEHAVIOR				
TREMORS	0	2	3	0
DISORIENTED	0	1	5	0
INACTIVE	3	3	3	2
HYPERACTIVE	0	1	1	0
IRRITABLE	0	0	1	0
RESPIRATION				
INCREASED RESPIRATORY RATE	0	0	2	2
OCULAR				
PALE EYES	0	0	2	0
INJECTION SITE REACTION				
BRUISE	0	3	5	0
FLUID DISCHARGE	0	0	1	0
BLOOD DRAINAGE	0	0	2	0
FOOD CONSUMPTION				
DECREASED APPETITE	0	0	1	0
DEATH	0	0	3	0

* Data presented as number of animals affected.

Table 2 (cont.)

CLINICAL OBSERVATIONS SUMMARY*

Group (n) Observation	RL (10)	HSD (10)	HS (10)	D70 (10)
	Females			
NORMAL/NO SIGNIFICANT SIGNS	4	0	0	0
BEHAVIOR				
TREMORS	0	2	4	1
DISORIENTED	1	7	5	3
INACTIVE	0	7	6	3
HYPERACTIVE	0	0	0	1
AGGRESSIVE	0	1	1	2
RESPIRATION				
INCREASED RESPIRATORY RATE	5	10	7	7
INJECTION SITE REACTION				
BRUISE	0	4	0	0
DRIED BLOODY MATERIAL	1	0	2	0
DISCOLORATION	1	1	0	1
NECROSIS	0	2	0	0
GASTROINTESTINAL				
DIARRHEA	0	1	0	0
REFLEXES				
INCREASED STARTLE REFLEX	1	0	0	0
DEATH	0	0	3	0

* Data presented as number of animals affected.

Table 3

GROUP MEAN BODY WEIGHT (kg)

Group	Day of Study -19	-13	-7	0	3†	7	14
			Male				
RL	2.87@	3.04	3.12	3.31	3.45	3.27	3.36
	±0.08	0.07	0.06	0.07	0.08	0.06	0.08
	(10)	(10)	(10)	(10)	(5)	(5)	(5)
HSD	2.89	3.06	3.20	3.30	3.40	3.30	3.38
	±0.07	0.09	0.08	0.08	0.07	0.15	0.15
	(10)	(10)	(10)	(10)	(5)	(5)	(5)
HS	2.88	3.10	3.21	3.33	3.42	3.32	3.41
	±0.07	0.06	0.06	0.06	0.09	0.09	0.12
	(10)	(10)	(10)	(10)	(3)	(4)	(4)
D70	2.87	3.03	3.16	3.26	3.37	3.33	3.38
	±0.06	0.06	0.07	0.06	0.11	0.06	0.04
	(10)	(10)	(10)	(10)	(5)	(5)	(5)

Group	Day of Study -29	-20	-14	-7	0	3†	14
			Female				
RL	3.16	3.42	3.61	3.82	3.95	4.05	4.02
	±0.08	0.09	0.09	0.10	0.10	0.16	0.16
	(10)	(10)	(10)	(10)	(10)	(5)	(5)
HSD	3.26	3.40	3.60	3.75	3.94	3.82	4.08
	±0.06	0.11	0.08	0.09	0.07	0.05	0.09
	(10)	(10)	(10)	(10)	(10)	(5)	(5)
HS	3.20	3.45	3.62	3.84	3.98	3.93	3.99
	±0.10	0.09	0.09	0.09	0.07	0.24	0.04
	(10)	(10)	(10)	(10)	(10)	(3)	(4)
D70	3.18	3.43	3.55	3.74	3.86	3.81	4.03
	±0.08	0.09	0.09	0.08	0.08	0.12	0.09
	(10)	(10)	(10)	(10)	(10)	(5)	(5)

† Day 3 body weights include only interim sacrifice animals.
@ Data are presented as mean ± standard error of the mean with the number of animals, n, in parenthesis.

Table 4

GROUP MEAN WATER CONSUMPTION (ml/day)

Group	Study Day -13	-7	1	2	3	4	5	6	7	14
					Male					
RL	292[@]	277	258	292	247	249	245	357	235	233
	±17	16	28	22	17	22	18	30		20
	(9)	(9)	(10)	(10)	(9)	(5)	(5)	(5)	(1)	(5)
HSD	320	338	311	276	263	267	300	356	NR	254
	±22	17	21	15	18	17	47	34		17
	(10)	(10)	(10)	(10)	(10)	(5)	(4)	(5)	(0)	(5)
HS	284	298	304	225	240	257	257	277	200	189
	±27	20	50	51	24	38	24	59	4	7
	(9)	(10)	(7)	(7)	(6)	(4)	(4)	(4)	(2)	(4)
D70	301	313	254	276	238	307	341	354	280	248
	±16	25	17	26	17	21	41	31		45
	(10)	(10)	(10)	(10)	(10)	(5)	(5)	(5)	(1)	(5)

Group	Study Day -14	-6	1	2	3	4	5	6	7	14
					Female					
RL	316	277	269	292	274	184	356	384	274	NR
	±21	27	29	26	33	37	32	31	41	
	(10)	(9)	(10)	(10)	(5)	(5)	(5)	(5)	(5)	(0)
HSD	325	315	367	295	321	188	343	356	312	NR
	±25	19	20	31	29	47	31	31	49	
	(10)	(10)	(10)	(10)	(5)	(5)	(5)	(5)	(5)	(0)
HS	333	324	332	279	300	281	369	389	359	NR
	±22	23	42	43	29	46	37	21	16	
	(10)	(10)	(7)	(7)	(4)	(4)	(4)	(4)	(4)	(0)
D70	307	309	324	297	295	200	301	376	316	NR
	±17	29	15	19	21	28	29	30	13	
	(10)	(10)	(10)	(10)	(4)	(5)	(5)	(5)	(5)	(0)

[@] Data are presented as mean ± standard error of the mean with the number of animals, n, in parenthesis.

Table 5

SERUM CHEMISTRY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					MALES								
ASPARTATE AMINO-	3	45.42	10.97	5	47.10	10.29	5	38.83	18.56	3	166.62	166.35	5
TRANSFERASE U/l	13	12.88	2.23	5	11.58	1.25	5	15.45	3.98	4	15.54	4.75	5
BLOOD UREA	3	19.14	5.05	5	20.14	1.84	5	14.93	2.65	3	21.80	5.78	5
NITROGEN mg/dl	13	17.68	1.79	5	17.48	1.81	5	16.03	1.84	4	16.20	0.97	5
CREATINE	3	1994.38	952.61	5	1413.39	181.98	5	1623.31	1031.82	3	4691.68	4902.42	5
PHOSPHOKINASE U/l	13	637.06	281.72	5	599.67	170.98	5	485.80	263.26	4	809.46	421.37	5
ALBUMIN	3	3.95	0.25	3	4.00	0.41	5	3.53	0.15	3	3.97	0.32	3
g/dL	13	4.82	0.18	5	4.52	0.18	5	4.55	0.13	4	4.94	0.26	5
TOTAL BILIRUBIN	3	0.00	0.00	5	0.00	0.00	5	0.00	0.00	3	0.00	0.00	5
mg/dl	13	0.00	0.00	5	0.00	0.00	5	0.00	0.00	4	0.00	0.00	5
CHLORIDE	3	106.80	3.03	5	108.20	1.48	5	103.33	1.53	3	105.20	2.78	5
Meq/dl	13	102.40	5.13	5	102.40	1.95	5	103.75	1.26	4	103.60	3.85	5
GLUCOSE	3	170.86	47.64	5	157.56	17.09	5	181.93	19.32	3	177.08	103.81	5
mg/dl	13	112.38	15.71	5	120.86	30.69	5	107.58	6.60	4	118.16	18.61	5
IRON	3	193.40	42.07	5	191.80	22.33	5	65.67†	21.50	3	225.60	58.16	5
µg/dl	13	145.20	33.66	5	163.80	41.76	5	141.50	57.02	4	136.80	30.03	5

† Mean value of the group is significantly different from that of the control at p = 0.01.

Table 5 (cont.)

SERUM CHEMISTRY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					MALES								
GAMMA GLUTAMYL	3	7.40	2.01	5	7.10	1.28	5	7.87	3.68	3	4.22	0.89	5
TRANSFERASE U/l	13	8.24	0.92	5	8.24	2.52	5	10.00	3.43	4	9.30	2.01	5
ALKALINE	3	82.14	33.57	5	113.56	27.14	5	42.07	5.60	3	138.12	72.33	5
PHOSPHATASE U/l	13	105.10	34.88	5	81.00	21.81	5	85.78	49.51	4	96.48	20.90	5
LACTATE	3	385.78	162.43	5	328.40	104.87	5	356.03	96.69	3	541.02	164.48	5
DEHYDROGENASE U/l	13	110.98	53.56	5	88.40	27.56	5	96.28	49.34	4	145.80	84.89	5
MAGNESIUM	3	2.18	0.24	5	2.25	0.20	5	1.96	0.14	3	2.32	0.13	5
mg/dl	13	2.05	0.17	5	1.85	0.08	5	1.99	0.26	4	2.07	0.24	5
SODIUM	3	149.42	1.73	5	150.02	1.07	5	147.47	0.78	3	149.54	5.98	5
Meq/l	13	146.38	4.23	5	145.04	0.50	5	146.85	2.90	4	148.34	2.72	5
CALCIUM	3	12.76	0.38	5	13.10	0.27	5	12.83	0.21	3	12.58	0.74	5
mg/dl	13	14.18	0.11	5	14.08	0.40	5	14.10	0.29	4	14.54	0.18	5
PHOSPHORUS	3	5.48	0.67	5	5.50	0.45	5	5.07	0.78	3	5.26	0.91	5
mg/dl	13	3.80	0.55	5	3.92	0.55	5	3.88	0.46	4	3.96	0.65	5
CHOLESTEROL	3	21.34	5.85	5	28.24	6.09	5	51.80	40.46	3	19.66	10.69	5
mg/dl	13	24.60	8.27	5	27.48	5.67	5	30.50	22.58	4	21.88	8.76	5

Table 5 (cont.)

SERUM CHEMISTRY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					MALES								
CREATININE	3	0.96	0.18	5	1.16	0.21	5	0.90	0.20	3	1.02	0.04	5
mg/dl	13	1.04	0.15	5	1.12	0.11	5	1.15	0.10	4	1.16	0.19	5
ALANINE AMINO-	3	38.72	11.50	5	52.24	9.23	5	47.93	10.95	3	69.32	44.08	5
TRANSFERASE U/l	13	51.00	9.57	5	28.54†	5.35	5	36.35*	3.23	4	39.50	11.13	5
TOTAL PROTEIN	3	4.70	0.65	3	5.04	0.45	5	4.70	0.26	3	5.17	0.21	3
g/dl	13	6.56	0.28	5	6.28	0.30	5	6.47	0.37	4	6.66	0.28	5
URIC ACID	3	0.10	0.07	5	0.12	0.08	5	0.07	0.12	3	0.14	0.09	5
mg/dl	13	0.04	0.05	5	0.00	0.00	5	0.03	0.05	4	0.00	0.00	5
POTASSIUM	3	5.12	0.52	5	5.18	0.58	5	4.87	0.51	3	6.06	2.34	5
Meq/l	13	4.44	0.42	5	4.34	0.58	5	4.35	0.60	4	4.40	0.39	5
TRIGLYCERIDE	3	76.60	6.84	5	124.60*	35.11	5	114.33*	13.20	3	138.20*	44.46	5
mg/dl	13	179.00	114.16	5	107.20	45.43	5	82.50	22.25	4	121.60	47.17	5
ALBUMIN-	3	6.90	4.12	3	4.16	1.33	5	3.23	1.33	3	3.67	1.59	3
GLOBULIN RATIO	13	2.88	0.62	5	2.56	0.30	5	2.43	0.34	4	2.84	0.39	5

† Mean value of the group is significantly different from that of the control at $p = 0.01$.
* Mean value of the group is significantly different from that of the control at $p = 0.05$.

Table 5 (cont.)

SERUM CHEMISTRY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					FEMALES								
ASPARTATE AMINO-	3	33.86	12.42	5	64.10	74.79	5	29.03	5.35	3	38.04	17.21	5
TRANSFERASE U/l	13	16.04	7.84	5	13.14	1.19	5	14.45	4.40	4	17.20	13.72	5
BLOOD UREA	3	20.52	1.73	5	19.28	2.33	5	18.23	2.80	3	17.50	1.61	5
NITROGEN mg/dl	13	22.52	3.31	5	23.60	3.05	5	20.50	5.55	4	20.88	1.35	5
CREATINE	3	2013.34	737.41	5	1900.74	805.37	5	2316.11	1030.59	3	1055.75	377.79	5
PHOSPHOKINASE U/l	13	653.04	305.65	5	871.54	321.11	5	552.53	187.11	4	634.86	418.66	5
ALBUMIN	3	4.20	0.20	3	3.78	0.10	4	3.73	0.32	3	3.80	0.30	5
g/dl	13	5.00	0.34	5	4.68	0.22	5	4.80	0.29	4	4.98	0.30	4
TOTAL BILIRUBIN	3	0.00	0.00	5	0.00	0.00	5	0.00	0.00	3	0.00	0.00	5
mg/dl	13	0.01	0.01	5	0.00	0.00	5	0.00	0.00	4	0.00	0.00	5
CHLORIDE	3	105.60	3.36	5	101.60	2.88	5	104.67	2.52	3	104.60	7.77	5
Meq/l	13	110.60	4.51	5	110.00	3.74	5	106.75	3.30	4	110.80	3.56	5
GLUCOSE	3	124.82	33.91	5	159.36	58.65	5	177.67	17.93	3	127.78	33.98	5
mg/dl	13	119.92	10.50	5	107.68	6.21	5	109.80	10.33	4	115.48	11.41	5
IRON	3	173.60	57.77	5	197.20	61.25	5	133.67	63.52	3	175.40	13.20	5
µg/dl	13	212.00	39.13	5	171.00	18.47	5	148.50	27.54	4	202.20	70.56	5

Table 5 (cont.)

SERUM CHEMISTRY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					FEMALES								
GAMMA GLUTAMYL	3	4.56	1.09	5	12.54	6.41	5	6.47	3.19	3	4.68	1.80	5
TRANSFERASE U/l	13	6.98	1.74	5	7.66	1.42	5	8.38	2.16	4	4.50	1.67	5
ALKALINE	3	55.86	25.39	5	81.04	35.10	5	38.40	15.40	3	79.14	19.09	5
PHOSPHATASE U/l	13	87.24	9.21	5	46.62	11.89	5	74.22	21.63	4	82.22	49.86	5
LACTATE	3	558.92	254.56	5	445.66	270.41	5	440.50	133.30	3	344.40	73.95	5
DEHYDROGENASE U/l	13	140.16	59.01	5	172.20	59.31	5	100.53	36.51	4	273.28	400.25	5
MAGNESIUM	3	2.55	0.23	5	2.19	0.28	5	2.01*	0.13	3	2.30	0.20	5
mg/dl	13	1.95	0.22	5	1.96	0.21	5	2.01	0.11	4	2.07	0.24	5
SODIUM	3	147.98	2.35	5	145.74	1.08	5	146.83	0.74	3	143.04	6.37	5
Meq/l	13	143.28	2.97	5	145.12	2.69	5	142.75	3.28	4	145.88	1.09	5
CALCIUM	3	11.88	0.83	5	11.62	0.28	5	11.97	0.06	3	12.02	0.19	5
mg/dl	13	14.16	0.24	5	12.44	3.10	5	13.88	0.62	4	14.42	0.28	5
PHOSPHORUS	3	4.90	0.52	5	4.74	0.48	5	4.53	0.42	3	4.44	0.42	5
mg/dl	13	3.86	0.50	5	3.26	0.49	5	3.92	0.30	4	3.68	0.31	5
CHOLESTEROL	3	65.24	25.83	5	49.84	8.07	5	58.00	12.62	3	42.04	19.68	5
mg/dl	13	55.12	14.57	5	60.76	14.66	5	71.30	10.91	4	55.32	21.61	5

* Mean value of the group is significantly different from that of the control at $p = 0.05$.

Table 5 (cont.)

SERUM CHEMISTRY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					FEMALES								
CREATININE	3	1.10	0.19	5	1.04	0.15	5	0.90	0.20	3	1.00	0.14	5
mg/dl	13	1.08	0.08	5	1.20	0.16	5	1.15	0.19	4	1.10	0.22	5
ALANINE AMINO-	3	35.14	7.82	5	60.06	22.94	5	27.90	3.03	3	38.02	9.09	5
TRANSFERASE U/l	13	45.56	11.54	5	32.26	3.17	5	43.45	17.40	4	36.28	11.79	5
TOTAL PROTEIN	3	5.77	0.31	3	4.90	0.51	4	5.13	0.40	3	5.00	0.34	5
g/dl	13	6.70	0.21	5	6.64	0.31	5	6.68	0.34	4	6.98	0.37	4
URIC ACID	3	0.00	0.00	5	0.00	0.00	5	0.03	0.06	3	0.00	0.00	5
mg/dl	13	0.06	0.05	5	0.04	0.05	5	0.08	0.05	4	0.02	0.04	5
POTASSIUM	3	5.52	1.94	5	5.04	0.57	5	4.80	0.40	3	7.54	6.34	5
Meq/l	13	4.68	0.77	5	4.64	0.23	5	4.30	0.36	4	5.00	1.07	5
TRIGLYCERIDE	3	65.60	26.56	5	52.20	17.08	5	106.00	45.64	3	55.40	19.06	5
mg/dl	13	70.20	30.64	5	67.60	23.08	5	74.75	20.63	4	106.40	65.52	5
ALBUMIN-	3	2.80	0.50	3	4.20	2.60	4	2.57	0.15	3	3.18	0.82	5
GLOBULIN RATIO	13	3.02	0.57	5	2.46	0.55	5	2.70	0.64	4	2.83	1.22	4

Table 6

HEMATOLOGY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					MALES								
WHITE BLOOD CELL	3	4.00	2.19	5	5.10	0.57	5	4.25	1.91	2	4.44	1.49	5
COUNT $X10^3$	13	7.52	1.76	5	7.80	2.43	5	10.65	2.77	4	8.40	1.64	5
RED BLOOD CELL	3	5.75	0.32	5	5.43	0.33	5	4.90*	0.38	2	6.07	0.33	5
COUNT $X10^6$	13	6.07	0.57	5	5.65	0.87	5	6.08	0.58	4	6.03	0.63	5
HEMOGLOBIN	3	12.14	0.91	5	11.76	0.69	5	10.75	0.07	2	12.42	0.70	5
g/dl	13	13.54	1.23	5	12.78	1.58	5	14.35	1.17	4	13.46	0.94	5
HEMATOCRIT	3	37.66	2.07	5	36.78	2.62	5	33.15	0.49	2	40.56	2.18	5
%	13	40.54	3.19	5	38.14	4.80	5	42.28	3.37	4	40.50	2.80	5
MEAN CORPUSCULAR	3	65.54	0.85	5	67.72	2.63	5	67.80	4.24	2	66.86	1.33	5
VOLUME fl	13	66.90	2.19	5	67.76	2.98	5	69.63	1.54	4	67.36	3.05	5
MEAN CORPUSCULAR	3	21.14	0.83	5	21.68	0.97	5	22.00	1.56	2	20.48	1.37	5
HEMOGLOBIN pg	13	22.34	0.63	5	22.74	1.17	5	23.63	0.84	4	22.40	1.04	5
MEAN CORPUSCULAR	3	32.22	1.03	5	32.02	0.63	5	32.40	0.28	2	30.66	1.72	5
HEMOGLOBIN CONC. g/dl	13	33.60	0.55	5	33.52	0.33	5	33.95	0.83	4	33.24	0.32	5

* Mean value of the group is significantly different from that of the control at $p = 0.05$.

Table 6 (cont.)

HEMATOLOGY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
						MALES							
PLATELET COUNT	3	262.20	111.83	5	335.80	115.83	5	440.50	84.15	2	536.00	293.75	5
$X10^3$	13	309.80	88.72	5	246.00	69.35	5	342.75	80.86	4	322.60	86.41	5
SEGMENTED	3	55.60	11.08	5	41.80	13.52	5	33.50	2.12	2	55.40	27.52	5
NEUTROPHILS	13	29.00	13.10	5	28.60	17.39	5	38.25	20.39	4	27.60	14.19	5
%													
BAND	3	0.00	0.00	5	0.00	0.00	5	0.00	0.00	2	0.00	0.00	5
NEUTROPHILS	13	0.20	0.45	5	0.00	0.00	5	0.00	0.00	4	0.20	0.45	5
%													
EOSINOPHILS	3	2.00	2.12	5	2.80	0.84	5	3.50	0.71	2	1.40	1.14	5
%	13	1.80	1.64	5	1.80	2.17	5	3.50	2.52	4	2.20	1.79	5
BASOPHILS	3	2.40	2.88	5	3.00	1.41	5	0.50	0.71	2	2.60	3.05	5
%	13	2.60	2.70	5	3.40	2.07	5	2.25	0.50	4	1.60	1.14	5
LYMPHOCYTES	3	32.60	13.90	5	44.80	10.85	5	58.50	2.12	2	33.20	29.47	5
%	13	56.80	15.87	5	60.20	19.98	5	44.75	26.42	4	61.60	13.16	5
MONOCYTES	3	2.20	2.39	5	1.60	1.52	5	2.00	1.41	2	2.40	1.95	5
%	13	2.00	1.41	5	1.00	1.73	5	3.00	2.16	4	3.20	2.68	5

Table 6 (cont.)

HEMATOLOGY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					MALES								
ATYPICAL LYMPHOCYTES %	3	5.20	1.30	5	6.00	3.46	5	2.00	1.41	2	5.40	3.91	5
	13	4.20	2.28	5	4.80	3.19	5	6.50	2.65	4	3.60	2.61	5
NRBC/100 WBC	3	3.40	3.05	5	6.00	3.08	5	4.00	0.00	2	7.00	3.46	5
	13	1.80	2.49	5	0.00	0.00	5	0.25	0.50	4	2.60	2.51	5
PROTHROMBIN TIME sec	3	9.50	0.00	1	-	-	-	-	-	-	-	-	-
	13	4.85	4.45	2	7.85	2.33	2	5.07	2.75	3	6.05	1.89	4
ACTIVATED PARTIAL THROMBOPLASTIN TIME sec	3	34.50	0.00	1	-	-	-	-	-	-	-	-	-
	13	18.60	1.27	2	40.90	0.00	1	23.20	18.70	3	25.35	15.37	4
RETICULOCYTES %	3	3.54	1.76	5	2.68	1.76	5	0.75	1.06	2	3.14	0.92	5
	13	3.88	0.48	5	2.20*	1.07	5	2.33	0.96	4	3.26	1.11	5

* Mean value of the group is significantly different from that of the control at p = 0.05.

Table 6 (cont.)

HEMATOLOGY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					FEMALES								
WHITE BLOOD CELL	3	3.73	1.53	3	3.83	2.45	4	1.53	0.67	3	6.13	0.55	3
COUNT $X10^3$	13	6.20	1.73	5	7.28	1.65	5	7.03	1.31	4	6.40	2.38	5
RED BLOOD CELL	3	4.74	0.50	3	4.73	0.52	4	4.07	0.87	3	4.62	0.24	3
COUNT $X10^6$	13	5.48	0.71	5	5.21	0.37	5	5.46	0.16	4	5.05	0.92	5
HEMOGLOBIN	3	11.20	0.70	3	10.80	1.00	4	9.53	1.76	3	10.77	0.72	3
g/dl	13	12.36	1.42	5	12.22	0.99	5	12.80	0.52	4	11.60	2.01	5
HEMATOCRIT	3	33.60	2.72	3	32.68	2.76	4	28.30	5.80	3	32.60	1.25	3
%	13	37.04	4.19	5	36.58	3.08	5	37.95	1.50	4	34.08	6.48	5
MEAN CORPUSCULAR	3	71.07	1.82	3	69.23	2.62	4	69.70	1.30	3	70.57	1.95	3
VOLUME fl	13	67.82	2.31	5	70.22	3.58	5	69.45	0.76	4	67.46	1.53	5
MEAN CORPUSCULAR	3	23.77	1.38	3	22.88	0.46	4	23.53	0.85	3	23.27	0.59	3
HEMOGLOBIN pg	13	22.62	0.70	5	23.48	0.92	5	23.43	0.32	4	23.00	0.57	5
MEAN CORPUSCULAR	3	33.40	1.32	3	33.03	0.78	4	33.77	0.81	3	33.00	1.67	3
HEMOGLOBIN CONC.	13	33.36	0.23	5	33.40	0.54	5	33.72	0.33	4	34.14	0.80	5
g/dl													

Table 6 (cont.)

HEMATOLOGY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					FEMALES								
PLATELET COUNT $X10^3$	3	410.67	164.45	3	237.25	130.71	4	251.00	330.74	3	325.00	166.14	3
	13	393.00	152.07	5	341.80	47.43	5	323.50	140.43	4	256.40	78.40	5
SEGMENTED NEUTROPHILS %	3	40.67	8.50	3	34.50	10.02	4	32.00	19.08	3	41.67	10.21	3
	13	41.00	16.17	5	40.20	17.91	5	51.25	8.38	4	42.40	15.49	5
BAND NEUTROPHILS %	3	0.00	0.00	3	0.00	0.00	4	0.00	0.00	3	0.00	0.00	3
	13	0.00	0.00	5	0.20	0.45	5	0.00	0.00	4	0.00	0.00	5
EOSINOPHILS %	3	2.00	1.00	3	1.25	1.50	4	0.33	0.58	3	1.00	1.00	3
	13	2.60	2.61	5	0.20	0.45	5	3.00	1.41	4	2.60	2.79	5
BASOPHILS %	3	2.00	1.73	3	1.75	2.36	4	2.00	2.00	3	1.00	1.73	3
	13	0.80	0.84	5	0.20	0.45	5	0.50	1.00	4	0.20	0.45	5
LYMPHOCYTES %	3	50.67	10.79	3	59.25	11.84	4	61.00	18.03	3	48.33	9.50	3
	13	38.60	11.08	5	40.20	17.60	5	39.25	6.02	4	50.00	15.12	5
MONOCYTES %	3	1.67	0.58	3	1.50	1.00	4	1.33	1.53	3	3.00	1.73	3
	13	2.40	2.51	5	1.60	1.52	5	3.75	4.27	4	0.80	0.84	5

Table 6 (cont.)

HEMATOLOGY SUMMARY

PARAMETER/ UNITS	STUDY DAY	RL MEAN	RL SD	RL N	HSD MEAN	HSD SD	HSD N	HS MEAN	HS SD	HS N	D 70 MEAN	D 70 SD	D 70 N
					FEMALES								
ATYPICAL	3	3.00	1.73	3	1.75	2.22	4	3.33	4.16	3	5.00	5.29	3
LYMPHOCYTES	13	6.20	3.35	5	2.00	1.00	5	2.25	1.71	4	4.00	3.81	5
%													
NRBC/100 WBC	3	0.00	0.00	3	0.00	0.00	4	0.00	0.00	3	0.00	0.00	3
	13	0.00	0.00	5	0.00	0.00	5	0.00	0.00	4	0.00	0.00	5
PROTHROMBIN TIME	3	7.00	0.00	1	6.65	0.21	2	-	-	-	-	-	-
sec	13	6.08	0.76	4	8.80*	0.00	2	6.30	0.61	3	8.50*	1.41	2
ACTIVATED PARTIAL	3	28.10	0.00	1	44.30	4.53	2	-	-	-	-	-	-
THROMBOPLASTIN TIME	13	9.03	6.83	4	19.45	7.42	2	12.73	10.58	3	6.55	7.00	2
sec													
RETICULOCYTES	3	3.97	1.10	3	3.05	1.26	4	4.23	0.74	3	2.73	1.10	3
%	13	3.44	0.57	5	5.04	1.74	5	2.88	1.36	4	4.88	2.69	5

* Mean value of the group is significantly different from that of the control at p = 0.05.

The bruising, discoloration, and necrosis around the injection site on the ear were observed in 7 animals receiving HSD and 5 animals receiving HS. Only 1 animal in each of the groups receiving D70 or RL exhibited any of these signs. This finding was consistent with observations made in a maximum tolerated dose study of HSD in mice in which tail sloughing was observed when HSD and HS were administered via the tail vein (17). These responses were attributed to unavoidable extravasation of injection fluid around the injection site. Since the injection technique was the same for all animals, one could assume that equivalent amounts of extravasation would occur in all dose groups. Therefore, the increased incidence of irritation in HSD and HS, but not in D70 treated animals, suggests that extravascular hypertonic saline causes tissue necrosis by a mechanism other than by an ischemic response due to increased extravascular fluid pressure. The probable mechanism for this local toxicity is a direct effect of the HS on extravascular tissues even though HS and HSD were no more irritating following paravenous administration than RL when evaluated for local irritation (18). However, the amount of fluid that was injected paravenously in the rabbit local irritation study was 0.1 ml which produced a wheal considerably smaller than that produced by the fluid that was extravasated in the rabbit maximum tolerated dose study.

In albino rabbits, the reddish color of the eyes is associated with the concentration of erythrocytes in the highly vascular retina; thus, the "pale eye" observation would suggest a reduction (or dilution) in the erythrocyte concentration. The increased incidence of pale eyes in the HS group compared with the RL group is attributed to the hyperosmotic action of the solution drawing additional fluid into the vascular compartment which results in a greater dilution of erythrocytes than the RL group.

With the exception of decreased serum iron in the HS group 3 days after administration, no consistent changes were seen in serum chemistry parameters, and no significant changes outside of normal limits were observed in the hematology parameters. Body weights and water consumption were unaffected by the dosing.

No significant treatment-related findings other than local toxicity around the injection site were observed at necropsy 3 or 14 days after administration of the fluids nor in the histological examination of selected tissues. This suggests that any morphological changes due to the administration of the volume expanders were transient, if any did occur.

These data suggest that the maximum tolerated dose of HSD administered intravenously over a 5-minute period is 20 ml/kg. The toxicity observed following HSD administration was attributable primarily to the HS component and is an expected physiological response to large volumes of hypertonic saline. The findings of lethality following HS administration suggests that the rabbit is more sensitive to the acute hemodynamic effects of HS than HSD. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate that there will be minimal adverse effects associated with the therapeutic administration of HSD.

CONCLUSION

The maximum tolerated dose of HSD following acute intravenous administration is 20 ml/kg, and the toxicity associated with the HSD administration is consistent with the administration of large volumes of hypertonic saline. Since the proposed therapeutic dose of HSD is only 4 ml/kg, these findings indicate that there will be minimal adverse effects associated with the therapeutic administration of HSD.

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Page

APPENDICES

Appendix A. Chemical Data.....32
Appendix B. Animal Data.....36
Appendix C. Historical Listing of Events.....37
Appendix D. Individual Animal Histories.....38
Appendix E. Body Weights.....66
Appendix F. Water Consumption.....70
Appendix G. Serum Chemistry.....74
Appendix H. Hematology.....87
Appendix I. Pathology Report.....96

Appendix A: CHEMICAL DATA

Pharmacia

CERTIFICATE OF ANALYSIS 1987-10-23

Product

6 % DEXTRAN 70 IN 7,5 %
SODIUM CHLORIDE INJECTION

Charge No. NC 54845

Inherent viscosity	27 ml/g
Absorbance (375 nm, 10 mm)	0,006
pH	4,6
Heavy metals	< 5 ppm
Sodium chloride	74,7 g/1000 ml
Dextran 70	60 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

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Analytical Chemistry Department

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Appendix A (cont.): CHEMICAL DATA

Pharmacia

Product

CERTIFICATE OF ANALYSIS 1988-12-19

7,5 % SODIUM CHLORIDE

Charge No. I 318712

Identification	passed test
Absorbance	0.000
pH	6.0
Heavy metals	< 5 ppm
Sodium chloride	75,0 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for biological trials.

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Analytical Chemistry Department

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Appendix A (cont.): CHEMICAL DATA

Pharmacia

Certificate of analysis

Name: **MACRODEX** 60 mg/ml in Normal saline

Item No.: 10-4510-00

Lot No.: NE 54941

Test		Result	Tolerance limit	Method
Inherent viscosity	ml/g	26	25 - 28	03700
Colour		0,01	Max. 0,04	03811
pH		4,9	4,0 - 7,0	USP XX p. 968
Heavy metals ppm		< 5	Max. 5	USP XX p. 909
Assay for				
- sodium chloride	g/1000ml	8,88	8,10 - 9,90	02355
- dextran 70	g/1000ml	59	54 - 66	02356
Sterility		Passed test	To pass test	02885
Pyrogens		Passed test	To pass test	02983

The identity is assured through strict adherence to established GMP rules throughout the manufacturing procedures.

Released for sale: 1987-05-25

Pharmacia AB
Quality Control Department

Mats Wiberg

M09

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Appendix A (cont.): CHEMICAL DATA

Pharmacia

CERTIFICATE OF ANALYSIS 1987-10-23

Product

LACTATED RINGER'S INJECTION

Charge No. NC 54847

pH	5,8
Heavy metals	< 5 ppm
Sodium	127 mmol/1000 ml
Potassium	3,91 mmol/1000 ml
Calcium	1,30 mmol/1000 ml
Chloride	105,5 mmol/1000 ml
Lactate	27,2 mmol/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

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Appendix B: ANIMAL DATA

Species: *Oryctolagus cuniculus*

Strain: New Zealand White

Source: Hazleton Research Products, Inc.
Swampbridge Road
Denver, PA 17517

Sex: Male and Female

Date of birth: 24 Apr 88

Method of randomization: Weight bias, stratified animal allocation (XYBION Medical Systems PATH/TOX AESLCT Program)

Animals in each group: 10 Males and 10 Females

Condition of animals at start of study: Normal

Body weight range at dosing:	Males	2.906 - 3.767 kg
	Females	3.413 - 4.411 kg

Identification procedures: Supplier ear tag with corresponding LAIR animal number

Pretest conditioning: Quarantine/acclimation 25 August 1988 to 12 and 19 September 1988, males and females, respectively

Justification: The laboratory rabbit is a standard laboratory model for acute toxicity studies and is accepted by all regulatory agencies.

Appendix C: HISTORICAL LISTING OF STUDY EVENTS

Date	Event
24 Aug 88	Animals arrived at LAIR. They were sexed, observed for illness, and caged in the GLP Suite. Eighty-two animals were assigned to the study.
25 Aug 88	Animals were identified (ear tag referenced to LAIR number).
25, 31 Aug 88 6, 13, 16, 20, 27 Sep, 4 Oct 88	Animals were weighed.
31 Aug, 6, 14-27 Sep 88	Water consumption was monitored.
26 Aug 88	Quality control animals were submitted for necropsy.
25 Aug 88- 3 Oct 88	Animals were observed twice daily.
31 Aug 88	Animals were randomized into groups.
13 (M), 20 (F) Sep 88	Animals were dosed beginning at 0900 hours. Observations were conducted one, two, and four hours after dosing.
26 Sep, 3 Oct 88	Day 13 blood samples were collected.
16, 23, 27 Sep, 4 Oct 88	Animals were observed for clinical signs at approximately 0730 hours. Animals were delivered to the Necropsy Suite for blood sampling (Day 3), euthanasia and necropsy.

Appendix D: INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00262	M/HS	0 / 09:20	DOSED	++
		0 / 09:26	FND DEAD	++
88F00301	M/HS	0 / 09:24	DOSED	++
		0 / 10:21	TREMORS	MODERATE
			DISORIENT	SLIGHT
		0 / 11:23	TREMORS	SLIGHT
			DISORIENT	SLIGHT
			INACTIVE	SLIGHT
		0 / 13:32	DISORIENT	SLIGHT
		1 / 11:10	NORMAL	
		2 / 09:05	NORMAL	
		3 / 07:00	N/EUTH	++
88F00282	M/HS	0 / 09:25	DOSED	++
		0 / 09:28	FND DEAD	++
88F00298	M/HS	0 / 10:07	DOSED	++
		0 / 11:07	INC RESP RATE	MODERATE
			HUNCHED	MODERATE
			INACTIVE	MODERATE
		0 / 12:08	INC RESP RATE	SLIGHT
			HUNCHED	SLIGHT
			INACTIVE	SLIGHT
		0 / 14:16	INC RESP RATE	SLIGHT
			HUNCHED	SLIGHT
			INACTIVE	SLIGHT
		1 / 11:10	HUNCHED	SLIGHT
		2 / 10:00	BRUISE	SEVERE LEFT EAR
			DISCHARGE	SLIGHT LEFT EAR
		3 / 07:00	BRUISE	SEVERE LEFT EAR
			EUTHAN	++
88F00257	M/HS	0 / 10:03	DOSED	++
		0 / 11:04	INACTIVE	SEVERE
			PALE EYES	MODERATE
			HUNCHED	MODERATE
		0 / 12:03	INACTIVE	MODERATE
			PALE EYES	MODERATE
			HUNCHED	SLIGHT
		0 / 14:17	INACTIVE	MODERATE
			PALE EYES	MODERATE
			HUNCHED	SLIGHT
		1 / 09:20	INACTIVE	SEVERE
			PALE EYES	MODERATE
			HUNCHED	SEVERE

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00257	M/HS	1 / 09:20	BRUISE	SEVERE LEFT EAR
		2 / 09:07	INACTIVE	SEVERE
			PALE EYES	MODERATE
			HUNCHED	SEVERE
			BRUISE	SEVERE LEFT EAR
		3 / 07:00	INACTIVE	SEVERE
			PALE EYES	MODERATE
			HUNCHED	SEVERE
			BRUISE	SEVERE LEFT EAR
			EUTHAN	++
88F00272	M/HS	0 / 10:51	DOSED	++
		0 / 10:55	FND DEAD	++
88F00280	M/HS	0 / 10:20	DOSED	++
		0 / 11:21	HUNCHED	MODERATE
			DISORIENT	SLIGHT
		0 / 12:19	HUNCHED	MODERATE
			DISORIENT	SLIGHT
		0 / 14:19	HUNCHED	SLIGHT
		1 / 11:26	HUNCHED	SLIGHT
		2 / 09:08	BRUISE	SLIGHT LEFT EAR
		3 / 10:10	BRUISE	SLIGHT LEFT EAR
		4 / 14:00	BRUISE	SLIGHT LEFT EAR
		5 / 11:00	BRUISE	SLIGHT LEFT EAR
		6 / 10:12	BRUISE	SLIGHT LEFT EAR
		7 / 10:40	NORMAL	
		8 / 13:35	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:53	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:38	NORMAL	
		14 / 07:00	N/EUTH	++
88F00303	M/HS	0 / 10:26	DOSED	++
		0 / 11:25	DISORIENT	MODERATE
			TREMORS	MODERATE
			HUNCHED	SLIGHT
		0 / 12:20	HUNCHED	SLIGHT
			DISORIENT	MODERATE
		0 / 14:25	NORMAL	
		1 / 11:10	NORMAL	
		2 / 10:01	NORMAL	
		3 / 10:37	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00303	M/HS	4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:18	NORMAL	
		7 / 10:52	NORMAL	
		8 / 13:24	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:03	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:43	NORMAL	
		14 / 07:00	N/EUTH	++
88F00254	M/HS	0 / 10:28	DOSED	++
		0 / 11:26	TREMORS	MODERATE
			DISORIENT	MODERATE
			HUNCHED	MODERATE
		0 / 12:25	HUNCHED	SLIGHT
			DISORIENT	SLIGHT
			TREMORS	SLIGHT
		0 / 14:28	DISORIENT	SLIGHT
			HUNCHED	SLIGHT
		1 / 11:26	HUNCHED	SLIGHT
		2 / 09:09	BRUISE	MODERATE LEFT EAR
		3 / 10:25	BRUISE	MODERATE LEFT EAR
			BLOOD DRN	SLIGHT LEFT EAR
		4 / 14:00	BRUISE	MODERATE LEFT EAR
			BLOOD DRN	SLIGHT LEFT EAR
		5 / 11:00	BRUISE	MODERATE LEFT EAR
		6 / 10:13	BRUISE	MODERATE LEFT EAR
		7 / 10:42	BRUISE	MODERATE LEFT EAR
		8 / 13:36	BRUISE	MODERATE LEFT EAR
		9 / 15:30	BRUISE	MODERATE LEFT EAR
		10 / 13:49	BRUISE	SLIGHT LEFT EAR
		11 / 09:30	BRUISE	SLIGHT LEFT EAR
		12 / 08:50	BRUISE	SLIGHT LEFT EAR
		13 / 14:35	BRUISE	SLIGHT LEFT EAR
		14 / 07:00	BRUISE	SLIGHT LEFT EAR
			EUTHAN	++
88F00297	M/HS	0 / 10:35	DOSED	++
		0 / 11:33	HUNCHED	MODERATE
			PALE EYES	SLIGHT
			DISORIENT	MODERATE
			INC RESP RATE	SLIGHT
		0 / 12:30	HUNCHED	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00297	M/HS	0 / 12:30	DISORIENT	SLIGHT
			INC RESP RATE	SLIGHT
			HYPERACT	MODERATE
		0 / 14:34	HYPERACT	MODERATE
		1 / 11:10	NORMAL	
		2 / 10:45	HYPERACT	SLIGHT
			BRUISE	MODERATE LEFT EAR
		3 / 11:06	HYPERACT	SLIGHT
			BRUISE	MODERATE LEFT EAR
			BLOOD DRN	SLIGHT LEFT EAR
		4 / 14:00	DEC APPET	MODERATE
		5 / 11:00	DEC APPET	MODERATE
		6 / 10:13	BRUISE	MODERATE LEFT EAR
		7 / 10:52	BRUISE	MODERATE LEFT EAR
		8 / 13:25	BRUISE	MODERATE LEFT EAR
			IRRITABLE	MODERATE
		9 / 15:30	BRUISE	MODERATE LEFT EAR
		10 / 13:59	BRUISE	SLIGHT LEFT EAR
		11 / 09:30	BRUISE	SLIGHT LEFT EAR
		12 / 08:50	BRUISE	SLIGHT LEFT EAR
		13 / 14:41	BRUISE	SLIGHT LEFT EAR
		14 / 07:00	BRUISE	SLIGHT LEFT EAR
			EUTHAN	++
88F00274	M/HSD	0 / 08:47	DOSED	++
		0 / 10:00	NORMAL	
		0 / 10:47	NORMAL	
		0 / 12:54	NORMAL	
		1 / 11:14	NORMAL	
		2 / 09:21	NORMAL	
		3 / 07:00	N/EUTH	++
88F00258	M/HSD	0 / 08:50	DOSED	++
		0 / 10:00	NORMAL	
		0 / 10:51	NORMAL	
		0 / 12:54	NORMAL	
		1 / 11:15	NORMAL	
		2 / 09:21	NORMAL	
		3 / 07:00	N/EUTH	++
88F00285	M/HSD	0 / 08:47	DOSED	++
		0 / 10:00	TREMORS	SEVERE
		0 / 10:49	TREMORS	MODERATE
			HYPERACT	SLIGHT
		0 / 12:55	TREMORS	MODERATE

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00285	M/HSD	0 / 12:55	HYPERACT	SLIGHT
		1 / 11:16	NORMAL	
		2 / 09:22	NORMAL	
		3 / 07:00	N/EUTH	++
88F00260	M/HSD	0 / 08:55	DOSED	++
		0 / 10:00	NORMAL	
		0 / 10:52	NORMAL	
		0 / 12:57	BRUISE	SEVERE LEFT EAR
		1 / 11:17	BRUISE	MODERATE LEFT EAR
		2 / 09:25	BRUISE	MODERATE LEFT EAR
		3 / 07:00	BRUISE	MODERATE LEFT EAR
			EUTHAN	++
88F00293	M/HSD	0 / 08:56	DOSED	++
		0 / 10:00	HUNCHED	SLIGHT
		0 / 10:56	HUNCHED	SLIGHT
		0 / 12:58	NORMAL	
		1 / 11:18	NORMAL	
		2 / 09:26	NORMAL	
		3 / 07:00	N/EUTH	++
88F00295	M/HSD	0 / 09:02	DOSED	++
		0 / 10:00	NORMAL	
		0 / 11:00	NORMAL	
		0 / 13:00	NORMAL	
		1 / 11:19	NORMAL	
		2 / 09:27	BRUISE	MODERATE RT EAR
		3 / 10:16	BRUISE	MODERATE RT EAR
		4 / 14:00	BRUISE	MODERATE RT EAR
		5 / 11:00	BRUISE	MODERATE RT EAR
		6 / 10:04	BRUISE	SLIGHT RT EAR
		7 / 10:43	BRUISE	SLIGHT RT EAR
		8 / 13:36	BRUISE	SLIGHT RT EAR
			INACTIVE	SLIGHT
		9 / 15:30	BRUISE	SLIGHT RT EAR
			INACTIVE	SLIGHT
		10 / 13:56	BRUISE	SLIGHT RT EAR
		11 / 09:30	BRUISE	SLIGHT RT EAR
		12 / 08:50	BRUISE	SLIGHT RT EAR
		13 / 14:41	BRUISE	SLIGHT RT EAR
		14 / 07:00	BRUISE	SLIGHT RT EAR
			EUTHAN	++
88F00289	M/HSD	0 / 09:06	DOSED	++
		0 / 10:00	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00289	M/HSD	0 / 11:06	NORMAL	
		0 / 13:10	NORMAL	
		1 / 11:19	NORMAL	
		2 / 09:29	NORMAL	
		3 / 10:17	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:07	NORMAL	
		7 / 10:43	NORMAL	
		8 / 13:37	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:55	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:39	NORMAL	
		14 / 07:00	N/EUTH	++
88F00290	M/HSD	0 / 09:10	DOSED	++
		0 / 10:00	NORMAL	
		0 / 11:08	NORMAL	
		0 / 13:11	BRUISE	SLIGHT LEFT EAR
		1 / 11:20	BRUISE	SLIGHT LEFT EAR
		2 / 09:30	BRUISE	SLIGHT LEFT EAR
		3 / 10:18	BRUISE	SLIGHT LEFT EAR
		4 / 14:00	BRUISE	SLIGHT LEFT EAR
		5 / 11:00	BRUISE	SLIGHT LEFT EAR
		6 / 10:07	BRUISE	SLIGHT LEFT EAR
			INACTIVE	SLIGHT
		7 / 10:44	BRUISE	SLIGHT LEFT EAR
			INACTIVE	SLIGHT
		8 / 13:38	BRUISE	SLIGHT LEFT EAR
			INACTIVE	SLIGHT
		9 / 15:30	BRUISE	SLIGHT LEFT EAR
		10 / 13:55	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:40	NORMAL	
		14 / 07:00	N/EUTH	++
88F00279	M/HSD	0 / 09:14	DOSED	++
		0 / 10:00	DISORIENT	MODERATE
			TREMORS	SLIGHT
		0 / 11:15	DISORIENT	SLIGHT
			TREMORS	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00279	M/HSD	0 / 13:15	DISORIENT	SLIGHT
			TREMORS	SLIGHT
		1 / 11:21	NORMAL	
		2 / 09:30	NORMAL	
		3 / 10:17	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:08	NORMAL	
		7 / 10:48	NORMAL	
		8 / 13:39	INACTIVE	SLIGHT
		9 / 15:30	NORMAL	
		10 / 13:52	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:38	NORMAL	
		14 / 07:00	N/EUTH	++
88F00263	M/HSD	0 / 09:14	DOSED	++
		0 / 10:00	HUNCHED	MODERATE
		0 / 11:14	HUNCHED	MODERATE
		0 / 13:15	HUNCHED	SLIGHT
		1 / 11:22	NORMAL	
		2 / 09:31	NORMAL	
		3 / 10:18	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:09	NORMAL	
		7 / 10:46	NORMAL	
		8 / 13:40	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:50	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:36	NORMAL	
		14 / 07:00	N/EUTH	++
88F00273	M/D70	0 / 11:14	DOSED	++
		0 / 12:15	INC RESP RATE	SLIGHT
		0 / 13:17	INC RESP RATE	SLIGHT
		0 / 16:06	NORMAL	
		1 / 11:03	NORMAL	
		2 / 09:34	NORMAL	
		3 / 07:00	N/EUTH	++

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00294	M/D70	0 / 11:06	DOSED	++
		0 / 12:10	NORMAL	
		0 / 13:06	NORMAL	
		0 / 16:03	NORMAL	
		1 / 11:28	NORMAL	
		2 / 09:32	NORMAL	
		3 / 07:00	N/EUTH	++
88F00265	M/D70	0 / 11:12	DOSED	++
		0 / 12:12	NORMAL	
		0 / 13:10	NORMAL	
		0 / 16:06	NORMAL	
		1 / 11:29	NORMAL	
		2 / 09:33	NORMAL	
		3 / 07:00	N/EUTH	++
88F00266	M/D70	0 / 11:26	DOSED	++
		0 / 12:25	NORMAL	
		0 / 13:29	NORMAL	
		0 / 16:07	NORMAL	
		1 / 11:31	NORMAL	
		2 / 12:40	NORMAL	
		3 / 07:00	N/EUTH	++
88F00267	M/D70	0 / 11:26	DOSED	++
		0 / 12:26	NORMAL	
		0 / 13:29	NORMAL	
		0 / 16:08	NORMAL	
		1 / 11:31	NORMAL	
		2 / 09:35	NORMAL	
		3 / 07:00	N/EUTH	++
88F00300	M/D70	0 / 11:33	DOSED	++
		0 / 12:30	NORMAL	
		0 / 13:32	NORMAL	
		0 / 16:08	NORMAL	
		1 / 11:10	NORMAL	
		2 / 09:51	NORMAL	
		3 / 10:32	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:14	NORMAL	
		7 / 10:53	INACTIVE	SLIGHT
		8 / 13:46	INACTIVE	SLIGHT
		9 / 15:30	INACTIVE	SLIGHT
		10 / 14:00	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00300	M/D70	11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:42	NORMAL	
		14 / 07:00	N/EUTH	++
88F00259	M/D70	0 / 11:34	DOSED	++
		0 / 12:30	NORMAL	
		0 / 13:33	NORMAL	
		0 / 14:09	NORMAL	
		1 / 11:31	NORMAL	
		2 / 09:35	NORMAL	
		3 / 10:20	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:03	NORMAL	
		7 / 10:47	NORMAL	
		8 / 13:40	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:50	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:36	NORMAL	
		14 / 07:00	N/EUTH	++
88F00292	M/D70	0 / 11:41	DOSED	++
		0 / 12:39	NORMAL	
		0 / 13:44	NORMAL	
		0 / 16:10	NORMAL	
		1 / 11:32	NORMAL	
		2 / 09:36	NORMAL	
		3 / 10:21	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:03	NORMAL	
		7 / 10:47	NORMAL	
		8 / 13:42	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:56	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:40	NORMAL	
		14 / 07:00	N/EUTH	++
88F00286	M/D70	0 / 11:45	DOSED	++
		0 / 12:45	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00286	M/D70	0 / 13:45	NORMAL	
		0 / 16:11	NORMAL	
		1 / 11:32	NORMAL	
		2 / 09:37	NORMAL	
		3 / 10:27	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:02	NORMAL	
		7 / 10:47	NORMAL	
		8 / 13:41	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:54	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:39	NORMAL	
		14 / 07:00	N/EUTH	++
88F00276	M/D70	0 / 11:49	DOSED	++
		0 / 12:47	INC RESP RATE	MODERATE
		0 / 13:48	INC RESP RATE	SLIGHT
		0 / 16:11	NORMAL	
		1 / 11:35	NORMAL	
		2 / 09:37	NORMAL	
		3 / 10:23	INACTIVE	SLIGHT
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:01	NORMAL	
		7 / 10:49	NORMAL	
		8 / 13:41	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:52	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:32	NORMAL	
		14 / 07:00	N/EUTH	++
88F00261	M/RL	0 / 11:54	DOSED	++
		0 / 12:55	NORMAL	
		0 / 13:55	NORMAL	
		0 / 16:30	NORMAL	
		1 / 11:09	NORMAL	
		2 / 09:42	NORMAL	
		3 / 07:00	N/EUTH	++

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00296	M/RL	0 / 12:02	DOSED	++
		0 / 13:01	NORMAL	
		0 / 14:01	NORMAL	
		0 / 16:31	NORMAL	
		1 / 11:10	NORMAL	
		2 / 09:48	NORMAL	
		3 / 07:00	N/EUTH	++
88F00277	M/RL	0 / 12:05	DOSED	++
		0 / 12:59	NORMAL	
		0 / 14:05	NORMAL	
		0 / 16:35	NORMAL	
		1 / 11:10	NORMAL	
		2 / 09:20	NORMAL	
		3 / 07:00	N/EUTH	++
88F00287	M/RL	0 / 12:10	DOSED	++
		0 / 13:09	NORMAL	
		0 / 14:14	NORMAL	
		0 / 16:34	NORMAL	
		1 / 11:11	NORMAL	
		2 / 09:43	NORMAL	
		3 / 07:00	N/EUTH	++
88F00281	M/RL	0 / 12:14	DOSED	++
		0 / 13:14	NORMAL	
		0 / 14:14	NORMAL	
		0 / 16:36	NORMAL	
		1 / 11:12	NORMAL	
		2 / 09:43	NORMAL	
		3 / 07:00	N/EUTH	++
88F00302	M/RL	0 / 12:19	DOSED	++
		0 / 13:19	NORMAL	
		0 / 14:18	NORMAL	
		0 / 16:32	NORMAL	
		1 / 11:10	NORMAL	
		2 / 09:48	NORMAL	
		3 / 10:32	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:18	INACTIVE	SLIGHT
		7 / 10:55	INACTIVE	SLIGHT
		8 / 13:47	INACTIVE	SLIGHT
		9 / 15:30	INACTIVE	SLIGHT
		10 / 14:01	INACTIVE	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00302	M/RL	11 / 09:30	INACTIVE	SLIGHT
		12 / 08:50	INACTIVE	SLIGHT
		13 / 14:42	INACTIVE	SLIGHT
		14 / 07:00	INACTIVE	SLIGHT
			EUTHAN	++
88F00283	M/RL	0 / 12:20	DOSED	++
		0 / 13:21	NORMAL	
		0 / 14:19	NORMAL	
		0 / 14:36	NORMAL	
		1 / 11:13	NORMAL	
		2 / 09:44	NORMAL	
		3 / 10:25	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:11	NORMAL	
		7 / 10:51	NORMAL	
		8 / 13:43	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:54	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:38	NORMAL	
		14 / 07:00	N/EUTH	++
88F00284	M/RL	0 / 12:25	DOSED	++
		0 / 13:24	NORMAL	
		0 / 14:24	NORMAL	
		0 / 14:37	NORMAL	
		1 / 11:13	NORMAL	
		2 / 09:44	NORMAL	
		3 / 10:26	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:11	NORMAL	
		7 / 10:51	NORMAL	
		8 / 13:43	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:53	INACTIVE	SLIGHT
		11 / 09:30	NORMAL	
		12 / 08:50	INACTIVE	SLIGHT
		13 / 14:39	INACTIVE	SLIGHT
		14 / 07:00	INACTIVE	SLIGHT
			EUTHAN	++

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00268	M/RL	0 / 12:29	DOSED	++
		0 / 13:29	NORMAL	
		0 / 14:29	NORMAL	
		0 / 16:28	NORMAL	
		1 / 11:07	NORMAL	
		2 / 09:40	NORMAL	
		3 / 10:23	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:09	NORMAL	
		7 / 10:49	NORMAL	
		8 / 13:44	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:51	INACTIVE	SLIGHT
		11 / 09:30	NORMAL	
		12 / 08:50	INACTIVE	SLIGHT
		13 / 14:36	NORMAL	
		14 / 07:00	N/EUTH	++
88F00269	M/RL	0 / 12:32	DOSED	++
		0 / 13:32	NORMAL	
		0 / 14:32	NORMAL	
		0 / 16:29	NORMAL	
		1 / 11:08	NORMAL	
		2 / 09:41	NORMAL	
		3 / 10:24	NORMAL	
		4 / 14:00	NORMAL	
		5 / 11:00	NORMAL	
		6 / 10:10	NORMAL	
		7 / 10:50	NORMAL	
		8 / 13:44	NORMAL	
		9 / 15:30	NORMAL	
		10 / 13:51	NORMAL	
		11 / 09:30	NORMAL	
		12 / 08:50	NORMAL	
		13 / 14:32	NORMAL	
		14 / 07:00	N/EUTH	++
88F00315	F/HS	0 / 08:35	DOSED	++
		0 / 08:38	FND DEAD	++
88F00339	F/HS	0 / 08:40	DOSED	++
		0 / 08:52	FND DEAD	++
88F00345	F/HS	0 / 08:45	DOSED	++

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00345	F/HS	0 / 09:45	INC RESP RATE	MODERATE
			INACTIVE	MODERATE
			HUNCHED	MODERATE
		0 / 10:45	INC RESP RATE	MODERATE
			INACTIVE	SEVERE
			HUNCHED	MODERATE
		0 / 12:45	INC RESP RATE	SLIGHT
			INACTIVE	MODERATE
			HUNCHED	MODERATE
		1 / 13:30	INACTIVE	SLIGHT
		2 / 14:15	INACTIVE	SLIGHT
		3 / 07:33	N/EUTH	++
88F00348	F/HS	0 / 09:00	DOSED	++
		0 / 10:00	DISORIENT	MODERATE
			TREMORS	MODERATE
			INC RESP RATE	MODERATE
		0 / 11:00	DISORIENT	MODERATE
			TREMORS	MODERATE
			INC RESP RATE	MODERATE
		0 / 13:00	HUNCHED	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:39	DRYBLOOD	MODERATE EAR
			EUTHAN	++
88F00332	F/HS	0 / 09:08	DOSED	++
		0 / 09:12	FND DEAD	++
88F00310	F/HS	0 / 09:12	DOSED	++
		0 / 10:12	INC RESP RATE	SEVERE
			INACTIVE	SEVERE
			HUNCHED	MODERATE
			DISORIENT	MODERATE
			TREMORS	MODERATE
		0 / 11:12	INC RESP RATE	SEVERE
			INACTIVE	SEVERE
			HUNCHED	MODERATE
			TREMORS	SLIGHT
		0 / 11:45	INC RESP RATE	MODERATE
			INACTIVE	MODERATE
			HUNCHED	MODERATE
		1 / 13:30	INACTIVE	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00310	F/HS	2 / 14:15	INACTIVE	SLIGHT
		3 / 06:52	INACTIVE	SLIGHT
			DRYBLOOD	MODERATE RT EAR
			EUTHAN	++
88F00331	F/HS	0 / 09:23	DOSED	++
		0 / 10:23	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			AGGRESIVE	MODERATE
		0 / 11:21	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			AGGRESIVE	SLIGHT
		0 / 13:22	HUNCHED	SLIGHT
			INC RESP RATE	MODERATE
			AGGRESIVE	MODERATE
		1 / 13:30	AGGRESIVE	SLIGHT
		2 / 14:15	AGGRESIVE	SLIGHT
		3 / 13:31	AGGRESIVE	SLIGHT
		4 / 09:30	AGGRESIVE	SLIGHT
		5 / 09:06	AGGRESIVE	SLIGHT
		6 / 14:52	INACTIVE	SLIGHT
		7 / 15:30	NORMAL	
		8 / 09:57	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:30	NORMAL	
		14 / 07:00	N/EUTH	++
88F00327	F/HS	0 / 09:24	DOSED	++
		0 / 10:24	INC RESP RATE	MODERATE
			DISORIENT	MODERATE
			TREMORS	MODERATE
			HUNCHED	MODERATE
		0 / 11:23	INC RESP RATE	MODERATE
			DISORIENT	MODERATE
			HUNCHED	MODERATE
		0 / 13:23	INC RESP RATE	SLIGHT
			HUNCHED	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	INACTIVE	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00327	F/HS	3 / 13:29	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	INACTIVE	SLIGHT
		6 / 14:51	INACTIVE	SLIGHT
		7 / 15:30	NORMAL	
		8 / 09:56	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:58	NORMAL	
		14 / 07:00	N/EUTH	++
88F00341	F/HS	0 / 09:31	DOSED	++
		0 / 10:31	INC RESP RATE	SEVERE
			INACTIVE	SEVERE
		0 / 11:31	INC RESP RATE	MODERATE
			INACTIVE	MODERATE
			HUNCHED	MODERATE
		0 / 13:31	HUNCHED	SLIGHT
			DISORIENT	MODERATE
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:35	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:54	NORMAL	
		7 / 15:30	NORMAL	
		8 / 10:02	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 15:06	NORMAL	
		14 / 07:00	N/EUTH	++
88F00305	F/HS	0 / 09:31	DOSED	++
		0 / 10:30	HUNCHED	MODERATE
			INACTIVE	SEVERE
			INC RESP RATE	SEVERE
		0 / 11:30	HUNCHED	MODERATE
			INACTIVE	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00305	F/HS	0 / 11:30	INC RESP RATE	SEVERE
			DISORIENT	MODERATE
			TREMORS	MODERATE
		0 / 13:31	HUNCHED	MODERATE
			INACTIVE	SLIGHT
		1 / 13:30	INACTIVE	SLIGHT
		2 / 14:15	NORMAL	
		3 / 13:23	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:46	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:49	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:52	NORMAL	
		14 / 07:00	N/EUTH	++
88F00313	F/HSD	0 / 09:38	DOSED	++
		0 / 10:30	DISORIENT	MODERATE
			INACTIVE	SEVERE
			INC RESP RATE	MODERATE
		0 / 11:38	INACTIVE	MODERATE
			INC RESP RATE	MODERATE
			HUNCHED	MODERATE
		0 / 13:38	INACTIVE	SLIGHT
			INC RESP RATE	SLIGHT
			HUNCHED	MODERATE
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 06:53	N/EUTH	++
88F00308	F/HSD	0 / 09:41	DOSED	++
		0 / 10:40	INC RESP RATE	MODERATE
			DISORIENT	SLIGHT
			HUNCHED	MODERATE
		0 / 11:40	INC RESP RATE	MODERATE
			DISORIENT	MODERATE
			HUNCHED	MODERATE
			INACTIVE	MODERATE
		0 / 13:40	INC RESP RATE	SLIGHT
			HUNCHED	MODERATE

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00308	F/HSD	0 / 13:40	INACTIVE	MODERATE
			AGGRESIVE	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 06:45	N/EUTH	++
88F00335	F/HSD	0 / 09:50	DOSED	++
		0 / 10:50	TREMORS	MODERATE
			HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		0 / 11:50	HUNCHED	MODERATE
			INC RESP RATE	SLIGHT
			DISORIENT	SLIGHT
		0 / 13:50	HUNCHED	SLIGHT
			DISORIENT	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:23	N/EUTH	++
88F00337	F/HSD	0 / 09:51	DOSED	++
		0 / 10:51	DISORIENT	MODERATE
			TREMORS	MODERATE
			INC RESP RATE	MODERATE
			HUNCHED	MODERATE
		0 / 11:51	INC RESP RATE	MODERATE
			HUNCHED	MODERATE
			INACTIVE	MODERATE
		0 / 13:51	INC RESP RATE	SLIGHT
			HUNCHED	MODERATE
			INACTIVE	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:28	DISCOLOR SLIGHT LEFT EAR DARK	
			EUTHAN	++
88F00349	F/HSD	0 / 09:58	DOSED	++
		0 / 10:57	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			INACTIVE	MODERATE
		0 / 11:55	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			INACTIVE	MODERATE
		0 / 13:58	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			INACTIVE	MODERATE

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00349	F/HSD	0 / 13:58	BRUISE	SEVERE LEFT EAR
		1 / 13:30	INACTIVE	SLIGHT
		2 / 14:15	NORMAL	
		3 / 07:48	N/EUTH	++
88F00334	F/HSD	0 / 10:05	DOSED	++
		0 / 11:05	INC RESP RATE	SEVERE
			DIARRHEA	MODERATE
			INACTIVE	MODERATE
		0 / 12:05	DIARRHEA	MODERATE
			INACTIVE	MODERATE
			HUNCHED	MODERATE
		0 / 14:05	DIARRHEA	MODERATE
			HUNCHED	MODERATE
			DISORIENT	MODERATE
		1 / 13:30	INACTIVE	SLIGHT
		2 / 14:15	INACTIVE	SLIGHT
		3 / 13:32	INACTIVE	SLIGHT
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:53	NORMAL	
		7 / 15:30	NORMAL	
		8 / 10:00	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:59	NORMAL	
		14 / 07:00	N/EUTH	++
88F00322	F/HSD	0 / 10:07	DOSED	++
		0 / 11:06	INC RESP RATE	MODERATE
			INACTIVE	MODERATE
		0 / 12:05	INC RESP RATE	SLIGHT
			INACTIVE	SLIGHT
			HUNCHED	SLIGHT
		0 / 14:06	INACTIVE	MODERATE
			HUNCHED	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:28	BRUISE	MODERATE LEFT EAR
		4 / 09:30	BRUISE	SLIGHT LEFT EAR
		5 / 09:05	BRUISE	SLIGHT LEFT EAR
		6 / 14:50	BRUISE	SLIGHT LEFT EAR

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00322	F/HSD	7 / 15:30	BRUISE	SLIGHT LEFT EAR
		8 / 09:55	BRUISE	SLIGHT LEFT EAR
		9 / 14:00	NECROSIS	SLIGHT LEFT EAR
		10 / 14:00	NECROSIS	SLIGHT LEFT EAR
		11 / 10:30	NECROSIS	SLIGHT LEFT EAR
		12 / 09:30	NECROSIS	SLIGHT LEFT EAR
		13 / 14:56	NECROSIS	SLIGHT LEFT EAR
		14 / 07:00	NECROSIS	SLIGHT LEFT EAR
			EUTHAN	++
88F00353	F/HSD	0 / 10:14	DOSED	++
		0 / 11:14	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		0 / 12:14	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			HUNCHED	SLIGHT
		0 / 14:17	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:37	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:56	BRUISE	SLIGHT LEFT EAR
		7 / 15:30	NORMAL	
		8 / 10:04	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 15:08	NORMAL	
		14 / 07:00	N/EUTH	++
88F00333	F/HSD	0 / 10:15	DOSED	++
		0 / 11:15	INC RESP RATE	MODERATE
			HUNCHED	MODERATE
			INACTIVE	SLIGHT
		0 / 12:15	INC RESP RATE	MODERATE
			HUNCHED	MODERATE
		0 / 14:14	INC RESP RATE	SLIGHT
			HUNCHED	SLIGHT
			BRUISE	MODERATE LEFT EAR
			DISORIENT	SLIGHT
		1 / 13:30	INACTIVE	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00333	F/HSD	2 / 14:15	INACTIVE	SLIGHT
		3 / 13:32	INACTIVE	SLIGHT
			HUNCHED	SLIGHT
		4 / 09:30	BRUISE	SLIGHT LEFT EAR
		5 / 09:05	BRUISE	SLIGHT LEFT EAR
		6 / 14:52	BRUISE	SLIGHT LEFT EAR
		7 / 15:30	BRUISE	SLIGHT LEFT EAR
		8 / 09:58	BRUISE	SLIGHT LEFT EAR
		9 / 14:00	NECROSIS	MODERATE LEFT EAR
			NECROSIS	SLIGHT RT EAR
		10 / 14:00	NECROSIS	MODERATE LEFT EAR
		11 / 10:30	NECROSIS	MODERATE LEFT EAR
		12 / 09:30	NECROSIS	MODERATE LEFT EAR
		13 / 14:58	NECROSIS	MODERATE LEFT EAR
		14 / 07:00	NECROSIS	MODERATE LEFT EAR
			EUTHAN	++
88F00318	F/HSD	0 / 10:26	DOSED	++
		0 / 11:26	DISORIENT	MODERATE
			HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		0 / 12:26	DISORIENT	MODERATE
			HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		0 / 14:26	DISORIENT	MODERATE
			HUNCHED	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:25	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:47	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:50	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:55	NORMAL	
		14 / 07:00	N/EUTH	++
88F00311	F/D70	0 / 10:28	DOSED	++
		0 / 11:[illegible]	HUNCHED	SEVERE
			INC RESP RATE	MODERATE

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00311	F/D70	0 / 11:27	DISORIENT	SEVERE
		0 / 12:27	HUNCHED	SEVERE
			INC RESP RATE	MODERATE
			DISORIENT	SEVERE
		0 / 14:28	HUNCHED	SLIGHT
			DISORIENT	SEVERE
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 06:52	N/EUTH	++
88F00314	F/D70	0 / 10:41	DOSED	++
		0 / 11:41	AGGRESIVE	MODERATE
			INC RESP RATE	MODERATE
			HUNCHED	SLIGHT
		0 / 12:41	AGGRESIVE	MODERATE
			INC RESP RATE	MODERATE
			HUNCHED	SLIGHT
		0 / 14:41	HUNCHED	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 06:55	N/EUTH	++
88F00338	F/D70	0 / 10:42	DOSED	++
		0 / 11:42	HUNCHED	MODERATE
			DISORIENT	SLIGHT
		0 / 12:42	HUNCHED	MODERATE
		0 / 14:42	HUNCHED	SLIGHT
			HYPERACT	MODERATE
		1 / 13:30	NORMAL	
		2 / 14:15	INACTIVE	SLIGHT
		3 / 07:28	N/EUTH	++
88F00344	F/D70	0 / 10:58	DOSED	++
		0 / 11:58	NORMAL	
		0 / 12:58	NORMAL	
		0 / 14:57	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:31	DISCOLOR	MODERATE EAR DARK
			EUTHAN	++
88F00347	F/D70	0 / 10:49	DOSED	++
		0 / 11:49	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		0 / 12:49	HUNCHED	MODERATE
			INC RESP RATE	MODERATE

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00347	F/D70	0 / 14:49	HUNCHED	MODERATE
			INC RESP RATE	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:07	N/EUTH	++
88F00319	F/D70	0 / 11:09	DOSED	++
		0 / 12:09	HUNCHED	SLIGHT
			TREMORS	SLIGHT
		0 / 13:11	HUNCHED	SLIGHT
		0 / 15:09	HUNCHED	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:26	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:49	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:54	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:56	NORMAL	
		14 / 07:00	N/EUTH	++
88F00304	F/D70	0 / 11:06	DOSED	++
		0 / 12:06	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
			DISORIENT	MODERATE
		0 / 13:06	HUNCHED	MODERATE
			INC RESP RATE	SLIGHT
			DISORIENT	MODERATE
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:37	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:56	NORMAL	
		7 / 15:30	NORMAL	
		8 / 10:05	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00304	F/D70	12 / 09:30	NORMAL	
		13 / 15:07	NORMAL	
		14 / 07:00	N/EUTH	++
88F00326	F/D70	0 / 11:16	DOSED	++
		0 / 12:16	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		0 / 13:14	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		0 / 15:16	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	INACTIVE	SLIGHT
		3 / 13:29	INACTIVE	SLIGHT
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:51	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:56	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:57	NORMAL	
		14 / 07:00	N/EUTH	++
88F00312	F/D70	0 / 11:17	DOSED	++
		0 / 12:17	HUNCHED	MODERATE
			INC RESP RATE	SLIGHT
		0 / 13:15	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		0 / 15:17	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:24	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:47	INACTIVE	SLIGHT
		7 / 15:30	NORMAL	
		8 / 09:49	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00312	F/D70	13 / 14:54	NORMAL	
		14 / 07:00	N/EUTH	++
88F00321	F/D70	0 / 11:24	DOSED	++
		0 / 12:24	INC RESP RATE	SLIGHT
			AGGRESIVE	MODERATE
		0 / 13:23	INC RESP RATE	SLIGHT
		0 / 15:24	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:27	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:49	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:55	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:56	NORMAL	
		14 / 07:00	N/EUTH	++
88F00323	F/RL	0 / 11:24	DOSED	++
		0 / 11:24	DISORIENT	MODERATE
		0 / 13:25	DISORIENT	MODERATE
		0 / 15:25	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 06:59	N/EUTH	++
88F00336	F/RL	0 / 11:31	DOSED	++
		0 / 12:31	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		0 / 13:30	HUNCHED	MODERATE
		1 / 13:30	HUNCHED	MODERATE
		2 / 14:14	NORMAL	
		3 / 07:27	DISCOLOR	SLIGHT LEFT EAR DARK
			DRYBLOOD	SLIGHT LEFT FOOT
			INC START	SLIGHT
			EUTHAN	++
88F00330	F/RL	0 / 11:37	DOSED	++
		0 / 12:35	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		0 / 13:37	HUNCHED	SLIGHT

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00330	F/RL	0 / 13:37	INC RESP RATE	SLIGHT
		0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:04	N/EUTH	++
88F00324	F/RL	0 / 11:38	DOSED	++
		0 / 12:36	HUNCHED	SLIGHT
			INC RESP RATE	MODERATE
		0 / 13:37	HUNCHED	SLIGHT
			INC RESP RATE	MODERATE
		0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:01	N/EUTH	++
88F00352	F/RL	0 / 11:44	DOSED	++
		0 / 12:44	NORMAL	
		0 / 13:44	NORMAL	
		0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 07:43	N/EUTH	++
88F00346	F/RL	0 / 11:45	DOSED	++
		0 / 12:44	NORMAL	
		0 / 13:45	NORMAL	
		0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:36	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:55	NORMAL	
		7 / 15:30	NORMAL	
		8 / 10:03	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 15:06	NORMAL	
		14 / 07:00	N/EUTH	++
88F00351	F/RL	0 / 11:50	DOSED	++
		0 / 12:50	NORMAL	
		0 / 13:48	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00351	F/RL	0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:36	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:55	NORMAL	
		7 / 15:30	NORMAL	
		8 / 10:03	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 15:08	NORMAL	
		14 / 07:00	N/EUTH	++
88F00325	F/RL	0 / 11:53	DOSED	++
		0 / 12:51	INC RESP RATE	MODERATE
		0 / 13:52	NORMAL	
		0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:28	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:50	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:56	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:57	NORMAL	
		14 / 07:00	N/EUTH	++
88F00307	F/RL	0 / 12:00	DOSED	++
		0 / 13:00	HUNCHED	MODERATE
			INC RESP RATE	MODERATE
		0 / 15:59	HUNCHED	SLIGHT
			INC RESP RATE	SLIGHT
		0 / 15:55	INC RESP RATE	SLIGHT
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:23	NORMAL	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

ANIMAL NUMBER	SEX/ GROUP	STUDY DAY/TIME DATA WAS TAKEN	CLINICAL SIGN	SEVERITY OR LOCATION
88F00307	F/RL	4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:46	NORMAL	
		7 / 15:30	NORMAL	
		8 / 09:49	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 14:53	NORMAL	
		14 / 07:00	N/EUTH	++
88F00340	F/RL	0 / 12:01	DOSED	++
		0 / 13:01	NORMAL	
		0 / 14:00	NORMAL	
		0 / 15:55	NORMAL	
		1 / 13:30	NORMAL	
		2 / 14:15	NORMAL	
		3 / 13:35	NORMAL	
		4 / 09:30	NORMAL	
		5 / 09:05	NORMAL	
		6 / 14:54	NORMAL	
		7 / 15:30	NORMAL	
		8 / 10:00	NORMAL	
		9 / 14:00	NORMAL	
		10 / 14:00	NORMAL	
		11 / 10:30	NORMAL	
		12 / 09:30	NORMAL	
		13 / 15:05	NORMAL	
		14 / 07:00	N/EUTH	++

Appendix E: BODY WEIGHTS (kg)

Animal	Day of Study -19	-13	-7	0	3	7	14
			RL Male				
88F00261#	2.95	2.98	2.92	3.33	3.35		
88F00296#	3.10	3.31	3.34	3.67	3.69		
88F00277#	3.22	3.35	3.28	3.43	3.48		
88F00287#	2.81	2.90	2.99	3.09	3.19		
88F00281#	2.99	3.05	3.27	3.54	3.53		
88F00302	2.73	2.92	3.03	3.17		3.30	3.27
88F00283	3.09	3.23	3.29	3.40		3.40	3.56
88F00284	2.47	2.73	2.81	2.98		3.10	3.12
88F00268	2.57	2.78	2.97	3.16		3.20	3.36
88F00269	2.73	3.14	3.32	3.37		3.37	3.48
Mean	2.87	3.04	3.12	3.31	3.45	3.27	3.36
Std.Dev	0.24	0.22	0.20	0.21	0.19	0.13	0.17
SEM	0.08	0.07	0.06	0.07	0.08	0.06	0.08
			HSD Male				
88F00274#	3.11	3.23	3.42	3.52	3.52		
88F00258#	2.74	3.01	3.14	3.23	3.32		
88F00285#	2.74	2.93	3.03	3.15	3.19		
88F00260#	2.92	3.01	3.23	3.30	3.38		
88F00293#	3.06	3.28	3.44	3.51	3.57		
88F00295	3.29	3.63	3.64	3.77		3.81	3.88
88F00289	2.68	2.79	3.06	3.12		3.20	3.29
88F00290	2.52	2.67	2.74	2.91		2.95	2.99
88F00279	2.84	2.91	2.96	3.15		3.12	3.19
88F00263	2.98	3.14	3.28	3.35		3.40	3.53
Mean	2.89	3.06	3.19	3.30	3.40	3.30	3.38
Std.Dev	0.23	0.27	0.26	0.25	0.15	0.33	0.34
SEM	0.07	0.09	0.08	0.08	0.07	0.15	0.15

Interim sacrifice animal

Appendix E (cont.): BODY WEIGHTS (kg)

Animal	Day of Study -19	-13	-7	0	3	7	14
			HS Male				
88F00262#	2.74	2.77	2.92	3.03	died		
88F00301#	3.00	3.25	3.32	3.41	3.41		
88F00282#	3.04	3.22	3.27	3.41	died		
88F00298#	2.76	3.01	3.12	3.28	3.29		
88F00257#	2.90	3.09	3.32	3.52	3.58		
88F00272	3.12	3.35	3.35	3.47	died		
88F00280	3.24	3.38	3.52	3.56		3.55	3.69
88F00303	2.45	2.89	3.03	3.12		3.18	3.26
88F00254	2.90	3.05	3.22	3.31		3.37	3.50
88F00297	2.66	2.96	3.07	3.17		3.18	3.20
Mean	2.88	3.10	3.21	3.33	3.42	3.32	3.41
Std.Dev	0.23	0.20	0.18	0.18	0.15	0.18	0.23
SEM	0.07	0.06	0.06	0.06	0.09	0.09	0.12
			D70 Male				
88F00273#	2.62	2.79	2.80	2.94	3.05		
88F00294#	2.75	2.98	3.12	3.23	3.20		
88F00265#	2.99	3.10	3.27	3.31	3.35		
88F00266#	3.08	3.33	3.48	3.54	3.68		
88F00267#	3.03	3.17	3.31	3.41	3.53		
88F00300	2.79	3.02	3.13	3.29		3.43	3.45
88F00259	2.61	2.76	2.87	3.05		3.17	3.23
88F00292	2.82	2.91	3.16	3.28		3.48	3.47
88F00286	3.16	2.96	3.05	3.19		3.19	3.33
88F00276	2.84	3.30	3.35	3.39		3.36	3.45
Mean	2.87	3.03	3.16	3.26	3.37	3.33	3.38
Std.Dev	0.19	0.19	0.21	0.17	0.25	0.14	0.10
SEM	0.06	0.06	0.07	0.06	0.11	0.06	0.04

Interim sacrifice animal

Appendix E (cont.): BODY WEIGHTS (kg)

Animal	Day of Study -29	-20	-14	-7	0	3	14
			RL Female				
88F00323#	3.35	3.75	3.87	4.16	4.28	4.34	
88F00336#	3.58	3.85	4.07	4.23	4.41	4.38	
88F00330#	3.15	3.53	3.68	3.93	4.12	4.10	
88F00324#	3.23	3.38	3.56	3.71	3.81	3.89	
88F00352#	2.96	3.20	3.28	3.44	3.52	3.54	
88F00346	3.22	3.60	3.85	4.19	4.22		4.50
88F00351	3.11	3.28	3.47	3.65	3.76		4.01
88F00325	3.04	3.30	3.57	3.80	4.01		4.09
88F00307	3.23	3.43	3.63	3.78	3.88		4.00
88F00340	2.67	2.89	3.14	3.34	3.48		3.51
Mean	3.16	3.42	3.61	3.82	3.95	4.05	4.02
Std.Dev	0.24	0.28	0.28	0.31	0.31	0.35	0.35
SEM	0.08	0.09	0.09	0.10	0.10	0.16	0.16
			HSD Female				
88F00313#	3.45	3.53	3.65	3.69	3.87	3.88	
88F00308#	3.23	3.32	3.46	3.61	3.85	3.75	
88F00335#	3.18	2.66	3.24	3.54	3.73	3.86	
88F00337#	3.30	3.40	3.40	3.26	3.72	3.66	
88F00349#	3.05	3.25	3.54	3.73	3.92	3.96	
88F00334	3.40	3.65	3.75	3.95	4.12		4.11
88F00322	3.23	3.31	3.56	3.70	3.75		3.82
88F00353	3.45	3.73	3.92	4.10	4.18		4.21
88F00333	3.47	3.86	4.00	4.21	4.36		4.34
88F00318	2.86	3.24	3.46	3.72	3.87		3.94
Mean	3.26	3.40	3.60	3.75	3.94	3.82	4.08
Std.Dev	0.20	0.33	0.24	0.28	0.21	0.12	0.21
SEM	0.06	0.11	0.08	0.09	0.07	0.05	0.09

Interim sacrifice animal

Appendix E (cont.): BODY WEIGHTS (kg)

Animal	Day of Study -29	-20	-14	-7	0	3	14
			HS Female				
88F00315#	2.71	3.19	3.48	3.67	3.88	died	
88F00339#	3.57	3.81	3.98	4.24	4.21	died	
88F00345#	3.73	3.94	4.13	4.37	4.41	4.42	
88F00348#	3.02	3.26	3.40	3.59	3.72	3.64	
88F00332	3.36	3.57	3.71	3.98	4.19	died	
88F00310#	3.17	3.35	3.42	3.70	3.77	3.74	
88F00331	2.97	3.28	3.37	3.64	3.80		4.03
88F00327	2.85	3.11	3.38	3.55	3.85		3.98
88F00341	3.15	3.40	3.57	3.71	3.88		3.88
88F00305	3.44	3.63	3.75	3.94	4.05		4.08
Mean	3.20	3.45	3.62	3.84	3.98	3.93	3.99
Std.Dev	0.33	0.27	0.27	0.28	0.23	0.42	0.08
SEM	0.10	0.09	0.09	0.09	0.07	0.24	0.04
			D70 Female				
88F00311#	3.00	2.95	3.06	3.23	3.41	3.44	
88F00314#	2.98	3.31	3.42	3.76	3.86	3.84	
88F00338#	2.80	3.16	3.22	3.53	3.60	3.64	
88F00344#	3.28	3.53	3.66	3.76	3.98	3.98	
88F00347#	3.22	3.57	3.74	3.96	4.05	4.13	
88F00319	3.43	3.76	3.80	3.91	4.00		4.09
88F00304	2.96	3.28	3.35	3.54	3.54		3.68
88F00326	3.59	3.89	4.05	4.05	4.22		4.25
88F00312	3.31	3.46	3.63	3.85	4.02		4.07
88F00321	3.25	3.39	3.60	3.81	3.94		4.07
Mean	3.18	3.43	3.55	3.74	3.86	3.81	4.03
Std.Dev	0.24	0.28	0.29	0.24	0.26	0.27	0.21
SEM	0.08	0.09	0.09	0.08	0.08	0.12	0.09

Interim sacrifice animal

Appendix F: WATER CONSUMPTION (ml/day)

Animal 88F00-	Study Day -13	-7	1	2	3	4	5	6	7	14
RL Male										
261#	SP@	307	250	340	209					
296#	294	286	429	310	279					
277#	330	308	211	211	178					
287#	378	SP	403	276	SP					
281#	327	348	271	444	256					
302	254	281	182	262	240	247	285	256	235	143
283	270	200	222	261	224	209	214	419	NR$	245
284	195	208	182	209	220	195	289	390	NR	216
268	290	288	230	314	361	317	204	399	NR	294
269	294	265	199	295	252	275	232	320	NR	269
Mean	292	277	258	292	247	249	245	357	235	233
Std.Dev	52	47	88	68	52	50	40	68		58
SEM	17	16	28	22	17	22	18	30		26
HSD Male										
274#	439	429	417	337	203					
258#	396	399	273	252	193					
285#	290	398	307	308	308					
260#	285	294	296	241	214					
293#	275	277	247	259	290					
295	335	322	391	248	254	233	247	337	NR	296
289	271	320	277	263	265	296	294	312	NR	249
290	260	317	254	241	231	225	SP	265	NR	194
279	402	339	401	379	379	313	435	432	NR	259
263	243	287	246	236	296	270	223	434	NR	273
Mean	320	338	311	276	263	267	300	356		254
Std.Dev	69	53	67	49	57	38	95	75		38
SEM	22	17	21	15	18	17	47	34		17

Interim sacrifice animal
@ Spill
$ Not recorded

Appendix F (cont.): WATER CONSUMPTION (ml/day)

Animal 88F00-	Study Day -13	-7	1	2	3	4	5	6	7	14
					HS Male					
262#	297	321	died							
301#	386	189	440	386	241					
282#	416	414	died							
298#	219	302	320	139	213					
257#	SP@	324	429	267	232					
272	319	322	died							
280	283	343	338	366	SP	358	320	414	NR$	178
303	206	250	248	156	159	177	206	156	204	183
254	263	256	306	251	257	226	263	329	NR	186
297	169	261	44	7	335	268	239	207	196	209
Mean	284	298	304	225	240	257	257	277	200	189
Std.Dev	82	62	133	134	58	77	48	117	6	14
SEM	27	20	50	51	24	38	24	59	4	7
					D70 Male					
273#	226	250	242	247	198					
294#	366	399	278	443	193					
265#	295	297	231	242	200					
266#	329	400	296	120	303					
267#	235	162	200	245	162					
300	297	306	255	242	296	277	259	277	280	270
259	343	316	253	293	287	336	338	327	NR	189
292	293	306	173	287	251	261	435	313	NR	179
286	264	264	249	282	203	287	242	440	NR	188
276	363	426	366	354	289	375	430	412	NR	416
Mean	301	313	254	276	238	307	341	354	280	248
Std.Dev	50	80	53	84	53	47	91	69		101
SEM	16	25	17	26	17	21	41	31		45

Interim sacrifice animal
@ Spill
$ Not recorded

Appendix F (cont.): WATER CONSUMPTION (ml/day)

Animal 88F00-	-14	-6	1	2	3	4	5	6	7	14
					Study Day					
					RL Female					
323#	351	340	387	329	NR$					
336#	391	258	406	435	NR					
330#	332	226	288	317	NR					
324#	331	NR	301	360	NR					
352#	240	195	169	204	NR					
346	423	456	366	351	362	280	435	453	436	NR
351	228	225	229	223	222	216	298	289	225	NR
325	302	257	194	226	327	158	428	449	253	NR
307	226	228	161	180	180	56	283	365	224	NR
340	340	312	193	290	278	211	334	363	231	NR
Mean	316	277	269	292	274	184	356	384	274	
Std.Dev	68	81	93	82	74	84	72	69	91	
SEM	21	27	29	26	33	37	32	31	41	
					HSD Female					
313#	155	170	325	202	NR					
308#	333	305	398	247	NR					
335#	350	388	417	427	NR					
337#	278	380	295	395	NR					
349#	370	311	378	288	NR					
334	423	311	431	437	400	324	448	408	392	NR
322	337	329	348	232	268	169	289	363	207	NR
353	306	303	359	254	274	241	342	304	215	NR
333	429	349	462	314	280	42	361	433	457	NR
318	271	303	260	151	381	163	276	270	291	NR
Mean	325	315	367	295	321	188	343	356	312	
Std.Dev	80	60	63	97	64	104	68	69	110	
SEM	25	19	20	31	29	47	31	31	49	

Interim sacrifice animal

$ Not recorded

Appendix F (cont.): WATER CONSUMPTION (ml/day)

Animal 88F00-	-14	-6	1	2	3	4	5	6	7	14
					Study Day					
					HS Female					
315	300	319	died							
339	363	341	died							
345#	330	323	471	354	NR$					
348#	211	167	172	158	NR					
332	419	345	died							
310#	250	321	239	140	NR					
331	431	323	419	468	400	416	464	448	335	NR
327	346	382	333	259	361	254	303	387	360	NR
341	373	446	263	308	283	244	393	369	405	NR
305	311	274	427	268	287	211	315	351	336	NR
Mean	333	324	332	279	333	281	369	389	359	
Std.Dev	69	72	112	113	57	92	75	42	33	
SEM	22	23	42	43	29	46	37	21	16	
					D70 Female					
311#	399	357	386	444	NR					
314#	3[illegible]7	403	392	280	NR					
338#	241	262	323	231	NR					
344#	293	360	331	265	NR					
347#	309	304	340	313	NR					
319	285	316	276	252	238	178	313	424	323	NR
304	369	462	349	340	335	237	217	441	356	NR
326	306	144	326	303	314	224	372	285	324	NR
312	281	268	245	248	SP	259	255	331	282	NR
321	229	212	268	297	294	100	349	401	296	NR
Mean	307	309	324	297	295	200	301	376	316	
Std.Dev	54	93	48	61	42	63	65	66	29	
SEM	17	29	15	19	21	28	29	30	13	

\# Interim sacrifice animal
$ Not recorded

Appendix G: SERUM CHEMISTRY

List of Serum Chemistry Abbreviations/Units

AST	Aspartate Amino-Transferase (U/l)
ALT	Alanine Amino-Transferase (U/l)
GGT	Gamma Glutamyl Transferase (U/l)
CK	Creatine Phosphokinase (U/l)
LDHL	Lactate Dehydrogenase (U/l)
ALK	Alkaline Phosphatase (U/l)
ALB	Albumin (g/dl)
BILI	Total Bilirubin (mg/dl)
CL	Chloride (Meq/l)
GLU	Glucose (mg/dl)
IRON	Iron (µg/dl)
MAG	Magnesium (mg/dl)
CAL	Calcium (mg/dl)
PHOS	Phosphorus (mg/dl)
CHOL	Cholesterol (mg/dl)
CR	Creatinine (mg/dl)
TP	Total Protein (g/dl)
URIC	Uric Acid (mg/dl)
NA	Sodium (Meq/l)
K	Potassium (Meq/l)
TRIG	Triglyceride (mg/dl)
BUN	Blood Urea Nitrogen (mg/dl)
A-G	Albumin/Globulin Ratio

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 1
ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDHL
88F00261	M	4/1	4	35.2	19.2	1808.6	3.9	0	108.	194.8	231.	4.3	75.5	343.9
88F00296	M	4/1	4	48.5	18.2	3594.2	3.7	0	108.	129.2	183.	7.1	55.0	484.5
88F00277	M	4/1	4	37.4	16.7	1169.62	3.9	0	102.	233.4	237.	7.6	65.8	349.2
88F00287	M	4/1	4	43.3	27.5	2001.5	4.3	0	110.	178.9	134.	9.8	140.4	160.6
88F00281	M	4/1	4	62.7	14.1	1398.00	NT	0	106.	118.0	182.	8.2	74.0	590.7
Parameter means:				45.42	19.14	1994.38	3.95	0.00	106.80	170.86	193.40	7.40	82.14	385.78
Standard deviations:				10.97	5.05	952.61	0.25	0.00	3.03	47.64	42.07	2.01	33.57	162.43
88F00274	M	2/1	4	49.2	21.5	1564.83	3.8	0	110.	168.6	205.	8.4	149.5	228.6
88F00258	M	2/1	4	46.4	19.7	1487.65	4.0	0	108.	158.1	216.	5.0	106.7	484.7
88F00285	M	2/1	4	31.0	17.2	1099.45	4.6	0	106.	156.9	177.	7.1	133.6	277.9
88F00260	M	2/1	4	59.5	20.5	1429.59	3.5	0	108.	129.9	200.	7.2	89.5	384.7
88F00293	M	2/1	4	49.4	21.8	1485.45	4.1	0	109.	174.3	161.	7.8	88.5	266.1
Parameter means:				47.10	20.14	1413.39	4.00	0.00	108.20	157.56	191.80	7.10	113.56	328.40
Standard deviations:				10.29	1.84	18[illegible].98	0.41	0.00	1.48	17.09	22.33	1.28	27.14	104.87
88F00301	M	1/1	4	59.8	14.9	834.84	3.7	0	102.	204.2	44.	11.9	47.2	360.9
88F00298	M	1/1	4	24.5	17.6	1245.98	3.5	0	103.	172.0	87.	7.0	42.9	257.0
88F00257	M	1/1	4	32.2	12.3	2791.1	3.4	0	105.	169.6	66.	4.7	36.1	450.2
Parameter means:				38.83	14.93	1623.31	3.53	0.00	103.33	181.93	65.67	7.87	42.07	356.03
Standard deviations:				18.56	2.65	1031.82	0.15	0.00	1.53	19.32	21.50	3.68	5.60	96.69
88F00273	M	3/1	4	449.7	29.6	3196.5	4.2	0	101.	135.9	237.	4.0	221.3	582.6
88F00294	M	3/1	4	65.4	16.5	2237.1	NT	0	108.	99.2	296.	3.9	213.2	688.7
88F00265	M	3/1	4	184.6	25.3	3116.9	4.[illegible]	0	104.	357.4	229.	5.7	86.4	479.0
88F00266	M	3/1	4	69.7	16.1	1532.21	3.6	0	106.	168.3	134.	4.2	81.7	286.7
88F00267	M	3/1	4	63.7	21.5	13375.7	NT	0	107.	124.6	232.	3.3	88.0	668.1
Parameter means:				166.62	21.80	4691.68	3.97	0.00	105.20	177.08	225.60	4.22	138.12	541.02
Standard deviations:				166.35	5.78	4902.42	0.32	0.00	2.78	103.81	58.16	0.89	72.33	164.48

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 2
ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL	L
88F00261	M	4/1	4	2.10	151.1	12.5	6.5	20.0	
88F00296	M	4/1	4	2.27	151.4	13.0	5.2	21.5	
88F00277	M	4/1	4	1.81	147.5	12.4	5.7	30.0	
88F00287	M	4/1	4	2.28	148.4	13.3	5.3	21.6	
88F00281	M	4/1	4	2.44	148.7	12.6	4.7	13.6	
Parameter means:				2.18	149.42	12.76	5.48	21.34	
Standard deviations:				0.24	1.73	0.38	0.67	5.85	
88F00274	M	2/1	4	1.93	148.8	13.1	5.7	26.5	
88F00258	M	2/1	4	2.43	150.9	12.9	5.1	32.8	
88F00285	M	2/1	4	2.22	149.9	13.5	6.2	26.2	
88F00260	M	2/1	4	2.29	149.2	12.8	5.2	20.1	
88F00293	M	2/1	4	2.39	151.3	13.2	5.3	35.6	
Parameter means:				2.25	150.02	13.10	5.50	28.24	
Standard deviations:				0.20	1.07	0.27	0.45	6.09	
88F00301	M	1/1	4	2.10	148.1	12.9	4.2	25.6	
88F00298	M	1/1	4	1.83	147.7	13.0	5.3	98.4	
88F00257	M	1/1	4	1.94	146.6	12.6	5.7	31.4	
Parameter means:				1.96	147.47	12.83	5.07	51.80	
Standard deviations:				0.14	0.78	0.21	0.78	40.46	
88F00273	M	3/1	4	2.38	148.5	12.3	5.7	13.6	
88F00294	M	3/1	4	2.36	158.6	11.6	5.9	16.6	
88F00265	M	3/1	4	2.36	142.0	12.4	5.8	13.3	
88F00266	M	3/1	4	2.08	148.1	13.5	3.7	38.6	
88F00267	M	3/1	4	2.40	150.5	13.1	5.2	16.2	
Parameter means:				2.32	149.54	12.58	5.26	19.66	
Standard deviations:				0.13	5.98	0.74	0.91	10.69	

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS II
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 1
ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88F00261	M	4/1	4	1.0	43.8	4.9	.1	4.5	85.	3.9
88F00296	M	4/1	4	1.0	50.6	4.0	.1	5.0	82.	12.1
88F00277	M	4/1	4	.9	19.8	4.4	0	5.7	74.	8.3
88F00287	M	4/1	4	1.2	38.7	5.5	.2	4.8	68.	3.3
88F00281	M	4/1	4	.7	40.7	NT	.1	5.6	74.	NT
Parameter means:				0.96	38.72	4.70	0.10	5.12	76.60	6.90
Standard deviations:				0.18	11.50	0.65	0.07	0.52	6.84	4.12
88F00274	M	2/1	4	1.4	48.3	5.6	.1	4.3	86.	2.1
88F00258	M	2/1	4	1.0	43.7	4.8	.2	5.6	148.	5.0
88F00285	M	2/1	4	.9	49.0	5.4	.0	5.0	173.	5.4
88F00260	M	2/1	4	1.2	52.4	4.5	.2	5.8	108.	3.6
88F00293	M	2/1	4	1.3	67.8	4.9	.1	5.2	108.	4.7
Parameter means:				1.16	52.24	5.04	0.12	5.18	124.60	4.16
Standard deviations:				0.21	9.23	0.45	0.08	0.58	35.11	1.33
88F00301	M	1/1	4	.7	58.8	4.5	0	4.3	117.	4.7
88F00298	M	1/1	4	1.1	48.1	4.6	0	5.3	126.	2.9
88F00257	M	1/1	4	.9	36.9	5.0	.2	5.0	100.	2.1
Parameter means:				0.90	47.93	4.70	0.07	4.87	114.33	3.23
Standard deviations:				0.20	10.95	0.26	0.12	0.51	13.20	1.33
88F00273	M	3/1	4	1.0	141.9	5.0	.1	4.4	132.	5.0
88F00294	M	3/1	4	1.0	43.7	NT	.1	8.4	87.	NT
88F00265	M	3/1	4	1.0	80.0	5.1	.3	8.8	140.	4.1
88F00266	M	3/1	4	1.1	46.6	5.4	.1	4.7	209.	1.9
88F00267	M	3/1	4	1.0	34.4	NT	.1	4.0	123.	NT
Parameter means:				1.02	69.32	5.17	0.14	6.06	138.20	3.67
Standard deviations:				0.04	44.08	0.21	0.09	2.34	44.46	1.59

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 5

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDHL
88F00323	F	4/2	4	20.4	19.8	1497.01	4.2	0	102.	156.2	222.	4.7	91.0	323.9
88F00336	F	4/2	4	30.2	20.0	2460.8	4.4	0	105.	155.8	210.	4.8	68.0	503.6
88F00330	F	4/2	4	25.4	19.6	2093.2	4.0	0	108.	129.0	160.	4.7	37.9	330.8
88F00324	F	4/2	4	50.1	19.6	2930.3	NT	0	110.	106.1	79.	5.8	56.1	903.2
88F00352	F	4/2	4	43.2	23.6	1085.40	NT	0	103.	77.0	197.	2.8	26.3	733.1
Parameter means:				33.86	20.52	2013.34	4.20	0.00	105.60	124.82	173.60	4.56	55.86	558.92
Standard deviations:				12.42	1.73	737.41	0.20	0.00	3.36	33.91	57.77	1.09	25.39	254.56
88F00313	F	2/2	4	35.8	17.7	1252.04	3.7	0	101.	145.1	242.	17.4	84.9	410.4
88F00308	F	2/2	4	197.6	16.4	1976.9	NT	0	102.	149.3	251.	20.6	48.5	895.4
88F00335	F	2/2	4	23.3	20.6	1433.78	3.9	0	101.	129.8	104.	5.7	60.1	228.2
88F00337	F	2/2	4	34.7	22.3	3260.0	3.8	0	98.	260.9	168.	11.8	72.8	241.6
88F00349	F	2/2	4	29.1	19.4	1581.00	3.7	0	106.	111.7	221.	7.2	138.9	452.7
Parameter means:				64.10	19.28	1900.74	3.78	0.00	101.60	159.36	197.20	12.54	81.04	445.66
Standard deviations:				74.79	2.33	805.37	0.10	0.00	2.88	58.65	61.25	6.41	35.10	270.41
88F00345	F	1/2	4	23.7	21.1	1217.04	4.1	0	107.	196.2	192.	9.9	55.8	289.7
88F00348	F	1/2	4	29.0	15.5	2470.5	3.5	0	102.	176.4	143.	5.9	26.5	489.2
88F00310	F	1/2	4	34.4	18.1	3260.8	3.6	0	105.	160.4	66.	3.6	32.9	542.6
Parameter means:				29.03	18.23	2316.11	3.73	0.00	104.67	177.67	133.67	6.47	38.40	440.50
Standard deviations:				5.35	2.80	1030.59	0.32	0.00	2.52	17.93	63.52	3.19	15.40	133.30
88F00311	F	3/2	4	68.3	15.9	1469.56	3.9	0	98.	129.7	162.	4.9	107.7	316.6
88F00314	F	3/2	4	32.3	16.6	741.33	4.1	0	117.	88.7	170.	2.9	59.1	441.0
88F00338	F	3/2	4	34.7	18.1	908.87	3.9	0	107.	100.2	197.	2.8	70.6	387.6
88F00344	F	3/2	4	27.1	16.9	1452.39	3.3	0	99.	170.9	177.	6.8	88.3	245.8
88F00347	F	3/2	4	27.8	20.0	706.60	3.8	0	102.	149.4	171.	6.0	70.0	331.0
Parameter means:				38.04	17.50	1055.75	3.80	0.00	104.60	127.78	175.40	4.68	79.14	344.40
Standard deviations:				17.21	1.61	377.79	0.30	0.00	7.77	33.98	13.20	1.80	19.09	73.95

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 6
ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL	L
88F00323	F	4/2	4	2.35	148.8	12.7	4.6	97.4	
88F00336	F	4/2	4	2.29	145.8	12.3	5.5	88.3	
88F00330	F	4/2	4	2.62	147.9	12.4	5.3	53.7	
88F00324	F	4/2	4	2.68	145.9	11.2	4.2	40.7	
88F00352	F	4/2	4	2.83	151.5	10.8	4.9	46.1	
Parameter means:				2.55	147.98	11.88	4.90	65.24	
Standard deviations:				0.23	2.35	0.83	0.52	25.83	
88F00313	F	2/2	4	2.03	146.4	11.8	4.2	59.1	
88F00308	F	2/2	4	2.28	145.9	11.3	4.4	45.8	
88F00335	F	2/2	4	2.03	145.2	11.5	5.0	49.9	
88F00337	F	2/2	4	2.07	144.2	12.0	4.7	38.7	
88F00349	F	2/2	4	1.92	147.0	11.5	5.4	55.7	
Parameter means:				2.19	145.74	11.62	4.74	49.84	
Standard deviations:				0.28	1.08	0.28	0.48	8.07	
88F00345	F	1/2	4	2.15	147.4	12.0	5.0	61.5	
88F00348	F	1/2	4	1.98	146.0	12.0	4.4	44.0	
88F00310	F	1/2	4	1.90	147.1	11.9	4.2	68.5	
Parameter means:				2.01	146.83	11.97	4.53	58.00	
Standard deviations:				0.13	0.74	0.06	0.42	12.62	
88F00311	F	3/2	4	2.42	147.2	11.7	3.7	30.2	
88F00314	F	3/2	4	2.22	131.8	12.1	4.6	67.1	
88F00338	F	3/2	4	2.59	144.5	12.2	4.7	33.7	
88F00344	F	3/2	4	2.19	145.2	12.1	4.5	20.9	
88F00347	F	3/2	4	2.10	146.5	12.0	4.7	58.3	
Parameter means:				2.30	143.04	12.02	4.44	42.04	
Standard deviations:				0.20	6.37	0.19	0.42	19.68	

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS II
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 3

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88F00323	F	4/2	4	1.1	31.2	6.1	0	4.8	72.	2.3
88F00336	F	4/2	4	.9	25.1	5.7	.0	4.7	48.	3.3
88F00330	F	4/2	4	1.1	46.3	5.5	0	3.4	101.	2.8
88F00324	F	4/2	4	1.0	36.6	NT	.0	6.2	32.	NT
88F00352	F	4/2	4	1.4	36.5	NT	0	8.5	75.	NT
Parameter means:				1.10	35.14	5.77	0.00	5.52	65.60	2.80
Standard deviations:				0.19	7.82	0.31	0.00	1.94	26.56	0.50
88F00313	F	2/2	4	1.1	79.5	4.2	0	5.0	52.	8.1
88F00308	F	2/2	4	1.0	87.5	NT	0	5.7	65.	NT
88F00335	F	2/2	4	1.1	38.8	5.4	.0	4.9	38.	2.8
88F00337	F	2/2	4	1.2	57.1	5.1	0	4.2	73.	2.8
88F00349	F	2/2	4	.8	37.4	4.9	0	5.4	33.	3.1
Parameter means:				1.04	60.06	4.90	0.00	5.04	52.20	4.20
Standard deviations:				0.15	22.94	0.51	0.00	0.57	17.08	2.60
88F00345	F	1/2	4	1.1	30.3	5.6	.1	4.4	55.	2.6
88F00348	F	1/2	4	.9	24.5	4.9	.0	4.8	143.	2.4
88F00310	F	1/2	4	.7	28.9	4.9	.0	5.2	120.	2.7
Parameter means:				0.90	27.90	5.13	0.03	4.80	106.00	2.57
Standard deviations:				0.20	3.03	0.40	0.06	0.40	45.64	0.15
88F00311	F	3/2	4	.9	35.4	5.4	.0	3.9	85.	2.7
88F00314	F	3/2	4	.9	43.6	5.2	0	18.8	64.	3.4
88F00338	F	3/2	4	.9	45.7	4.7	0	5.9	41.	4.5
88F00344	F	3/2	4	1.1	23.3	4.6	.0	4.6	41.	2.4
88F00347	F	3/2	4	1.2	42.1	5.1	.0	4.5	46.	2.9
Parameter means:				1.00	38.02	5.00	0.00	7.54	55.40	3.18
Standard deviations:				0.14	9.09	0.34	0.00	6.34	19.06	0.82

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 3
ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDHL
88F00302	M	4/1	14	13.5	20.1	550.86	5.1	0	106.	105.7	135.	7.0	85.0	74.0
88F00283	M	4/1	14	15.8	16.2	1115.19	4.7	0	100.	101.8	115.	9.2	71.6	205.2
88F00284	M	4/1	14	13.7	18.9	441.73	4.7	0	109.	111.9	203.	7.6	162.7	89.4
88F00268	M	4/1	14	10.1	15.9	429.34	4.7	0	101.	102.9	133.	8.5	105.7	85.1
88F00269	M	4/1	14	11.3	17.3	648.18	4.9	0	96.	139.6	140.	8.9	100.5	101.2
Parameter means:				12.88	17.68	637.06	4.82	0.00	102.40	112.38	145.20	8.24	105.10	110.98
Standard deviations:				2.23	1.79	281.72	0.18	0.00	5.13	15.71	33.66	0.92	34.88	53.56
88F00295	M	2/1	14	10.9	17.2	502.75	4.7	0	100.	119.7	218.	5.8	66.4	49.5
88F00289	M	2/1	14	10.1	15.9	655.66	4.7	0	101.	173.0	156.	6.5	106.7	113.7
88F00290	M	2/1	14	11.2	17.0	529.74	4.5	0	103.	104.0	158.	8.3	58.4	73.3
88F00279	M	2/1	14	13.2	20.6	871.17	4.4	0	103.	113.3	104.	8.3	71.7	113.8
88F00263	M	2/1	14	12.5	16.7	439.03	4.3	0	105.	94.3	183.	12.3	101.8	91.7
Parameter means:				11.58	17.48	599.67	4.52	0.00	102.40	120.86	163.80	8.24	81.00	88.40
Standard deviations:				1.25	1.81	170.98	0.18	0.00	1.95	30.69	41.76	2.52	21.81	27.56
88F00280	M	1/1	14	14.9	15.4	633.20	4.5	0	104.	98.7	182.	7.2	155.1	116.0
88F00303	M	1/1	14	20.4	15.5	157.86	4.4	0	105.	113.6	162.	12.5	84.4	34.8
88F00254	M	1/1	14	15.8	18.7	752.63	4.7	0	102.	111.4	165.	6.9	62.7	150.8
88F00297	M	1/1	14	10.7	14.5	399.49	4.6	0	104.	106.6	57.	13.4	40.9	83.5
Parameter means:				15.45	16.03	485.80	4.55	0.00	103.75	107.58	141.50	10.00	85.78	96.28
Standard deviations:				3.98	1.84	263.26	0.13	0.00	1.26	6.60	57.02	3.43	49.51	49.34
88F00300	M	3/1	14	11.6	17.4	413.98	5.2	0	100.	116.4	107.	9.1	74.5	72.2
88F00259	M	3/1	14	13.3	14.9	654.45	4.6	0	105.	92.1	133.	12.5	97.4	141.9
88F00292	M	3/1	14	13.4	15.7	604.54	5.2	0	99.	144.0	120.	7.7	126.1	100.7
88F00286	M	3/1	14	23.6	16.2	1505.33	4.8	0	107.	115.1	138.	7.5	79.0	290.3
88F00276	M	3/1	14	15.8	16.8	869.01	4.9	0	107.	123.2	186.	9.7	105.4	123.9
Parameter means:				15.54	16.20	809.46	4.94	0.00	103.60	118.16	136.80	9.30	96.48	145.80
Standard deviations:				4.75	0.97	421.37	0.26	0.00	3.85	18.61	30.03	2.01	20.90	84.89

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 4

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL
88F00302	M	4/1	14	2.22	150.7	14.3	3.6	19.7
88F00283	M	4/1	14	1.92	140.9	14.2	4.2	19.4
88F00284	M	4/1	14	1.87	150.4	14.0	3.1	28.5
88F00268	M	4/1	14	1.99	143.8	14.2	4.5	18.0
88F00269	M	4/1	14	2.25	146.1	14.2	3.6	37.4
Parameter means:				2.05	146.38	14.18	3.80	24.60
Standard deviations:				0.17	4.23	0.11	0.55	8.27
88F00295	M	2/1	14	1.85	144.3	14.2	3.9	30.0
88F00289	M	2/1	14	1.97	145.6	14.1	4.6	31.6
88F00290	M	2/1	14	1.85	145.3	14.3	3.8	28.0
88F00279	M	2/1	14	1.78	144.8	13.4	4.2	30.2
88F00263	M	2/1	14	1.79	145.2	14.4	3.1	17.6
Parameter means:				1.85	145.04	14.08	3.92	27.48
Standard deviations:				0.08	0.50	0.40	0.55	5.67
88F00280	M	1/1	14	1.78	142.7	13.8	4.5	20.7
88F00303	M	1/1	14	1.80	147.0	14.1	3.4	15.3
88F00254	M	1/1	14	2.35	148.9	14.0	3.9	21.9
88F00297	M	1/1	14	2.01	148.8	14.5	3.7	64.1
Parameter means:				1.99	146.85	14.10	3.88	30.50
Standard deviations:				0.26	2.90	0.29	0.46	22.58
88F00300	M	3/1	14	2.19	149.0	14.4	3.7	28.3
88F00259	M	3/1	14	1.99	147.1	14.7	3.5	20.1
88F00292	M	3/1	14	2.22	146.6	14.6	5.1	32.4
88F00286	M	3/1	14	2.27	152.8	14.7	3.9	18.6
88F00276	M	3/1	14	1.68	146.2	14.3	3.6	10.0
Parameter means:				2.07	148.34	14.54	3.96	21.[illegible]
Standard deviations:				0.24	2.72	0.18	0.65	8.76

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS II
Study Number: 88002

Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 2

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88F00302	M	4/1	14	1.1	44.5	6.5	0	5.1	148.	3.8
88F00283	M	4/1	14	1.0	59.1	6.3	.0	4.1	139.	2.9
88F00284	M	4/1	14	.8	63.0	6.9	.1	4.2	123.	2.1
88F00268	M	4/1	14	1.1	40.9	6.3	.1	4.2	104.	3.0
88F00269	M	4/1	14	1.2	47.5	6.8	.0	4.6	381.	2.6
Parameter means:				1.04	51.00	6.56	0.04	4.44	179.00	2.88
Standard deviations:				0.15	9.57	0.28	0.05	0.42	114.16	0.62
88F00295	M	2/1	14	1.3	34.4	6.7	.0	4.8	111.	2.3
88F00289	M	2/1	14	1.1	21.8	6.3	.0	5.1	91.	3.0
88F00290	M	2/1	14	1.0	24.4	6.4	0	3.9	184.	2.3
88F00279	M	2/1	14	1.1	32.6	6.1	0	3.8	73.	2.5
88F00263	M	2/1	14	1.1	29.5	5.9	0	4.1	77.	2.7
Parameter means:				1.12	28.54	6.28	0.00	4.34	107.20	2.56
Standard deviations:				0.11	5.35	0.30	0.00	0.58	45.43	0.30
88F00280	M	1/1	14	1.1	35.9	6.5	.1	3.5	56.	2.3
88F00303	M	1/1	14	1.1	34.8	6.0	.0	4.4	74.	2.7
88F00254	M	1/1	14	1.3	33.7	6.5	0	4.9	93.	2.7
88F00297	M	1/1	14	1.1	41.0	6.9	0	4.6	107.	2.0
Parameter means:				1.15	36.35	6.47	0.03	4.35	82.50	2.43
Standard deviations:				0.10	3.23	0.37	0.05	0.60	22.25	0.34
88F00300	M	3/1	14	1.1	57.6	6.9	0	4.5	172.	3.1
88F00259	M	3/1	14	1.1	36.6	6.6	0	4.4	72.	2.2
88F00292	M	3/1	14	1.3	27.3	7.0	0	4.9	172.	2.8
88F00286	M	3/1	14	1.4	36.3	6.4	0	3.8	101.	2.9
88F00276	M	3/1	14	.9	39.7	6.4	0	4.4	91.	3.2
Parameter means:				1.16	39.50	6.66	0.00	4.40	121.60	2.84
Standard deviations:				0.19	11.13	0.28	0.00	0.39	47.17	0.39

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 7
ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	AST	BUN	CK	ALB	BILI	CL	GLU	IRON	GGT	ALK	LDHL
88F00346	F	4/2	14	12.0	23.9	497.08	4.6	.03	107.	123.4	152.	8.2	71.8	74.9
88F00351	F	4/2	14	11.4	22.7	593.37	5.2	0	110.	123.6	198.	8.1	92.1	148.4
88F00325	F	4/2	14	9.7	17.8	413.97	4.7	0	107.	110.3	228.	7.7	86.3	84.1
88F00307	F	4/2	14	28.8	21.4	576.02	5.1	0	118.	133.8	255.	4.0	95.2	202.4
88F00340	F	4/2	14	18.3	26.8	1184.74	5.4	0	111.	108.5	227.	6.9	90.8	191.0
Parameter means:				16.04	22.52	653.04	5.00	0.01	110.60	119.92	212.00	6.98	87.24	140.16
Standard deviations:				7.84	3.31	305.65	0.34	0.01	4.51	10.50	39.13	1.74	9.21	59.01
88F00334	F	2/2	14	14.0	22.3	1240.52	4.4	0	111.	99.7	182.	8.1	43.9	259.2
88F00322	F	2/2	14	12.3	21.8	497.55	4.6	0	105.	112.2	142.	9.3	39.7	98.3
88F00353	F	2/2	14	13.6	28.0	584.07	5.0	0	111.	108.4	188.	8.2	36.1	152.2
88F00333	F	2/2	14	11.5	25.4	943.55	4.7	0	115.	103.3	164.	7.2	66.6	158.1
88F00318	F	2/2	14	14.3	20.5	1092.03	4.7	0	108.	114.8	179.	5.5	46.8	193.2
Parameter means:				13.14	23.60	871.54	4.68	0.00	110.00	107.68	171.00	7.66	46.62	172.20
Standard deviations:				1.19	3.05	321.11	0.22	0.00	3.74	6.21	18.47	1.42	11.89	59.31
88F00331	F	1/2	14	18.7	14.3	733.28	4.8	0	105.	107.4	124.	10.1	79.4	138.2
88F00327	F	1/2	14	8.4	21.3	298.47	5.2	0	103.	96.7	142.	8.5	102.6	53.0
88F00341	F	1/2	14	16.3	18.8	538.60	4.5	0	110.	120.9	140.	9.6	55.3	93.8
88F00305	F	1/2	14	14.4	27.6	639.79	4.7	0	109.	114.2	188.	5.3	59.6	117.1
Parameter means:				14.45	20.50	552.53	4.80	0.00	106.75	109.80	148.50	8.38	74.22	100.53
Standard deviations:				4.40	5.55	187.11	0.29	0.00	3.30	10.33	27.54	2.16	21.63	36.51
88F00319	F	3/2	14	40.8	22.8	1331.46	NT	0	116.	102.3	298.	2.3	121.7	983.7
88F00304	F	3/2	14	9.1	20.1	347.10	4.6	0	112.	108.6	117.	4.0	40.3	39.8
88F00326	F	3/2	14	6.5	19.7	294.71	4.9	0	111.	115.0	153.	5.3	27.7	52.3
88F00312	F	3/2	14	13.4	21.8	513.93	5.1	0	108.	132.4	234.	4.1	78.8	144.7
88F00321	F	3/2	14	16.2	20.0	687.08	5.3	0	107.	119.1	209.	6.8	142.6	145.9
Parameter means:				17.20	20.88	634.86	4.98	0.00	110.80	115.48	202.20	4.50	82.22	273.28
Standard deviations:				13.72	1.35	418.66	0.30	0.00	3.56	11.41	70.56	1.67	49.86	400.25

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS I
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 8

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	MAG	NA	CAL	PHOS	CHOL	L
88F00346	F	4/2	14	1.76	140.1	14.3	3.4	79.5	
88F00351	F	4/2	14	1.87	142.8	13.9	3.6	49.4	
88F00325	F	4/2	14	2.00	141.2	13.9	3.7	51.9	
88F00307	F	4/2	14	2.31	147.6	14.4	4.7	40.6	
88F00340	F	4/2	14	1.81	144.7	14.3	3.9	54.2	
Parameter means:				1.95	143.28	14.16	3.86	55.12	
Standard deviations:				0.22	2.97	0.24	0.50	14.57	
88F00334	F	2/2	14	2.15	143.0	13.9	3.1	38.3	
88F00322	F	2/2	14	2.16	146.5	6.9	4.1	72.4	
88F00353	F	2/2	14	1.65	145.4	13.7	2.8	56.4	
88F00333	F	2/2	14	1.90	148.7	13.7	3.2	61.8	
88F00318	F	2/2	14	1.94	142.0	14.0	3.1	74.9	
Parameter means:				1.96	145.12	12.44	3.26	60.76	
Standard deviations:				0.21	2.69	3.10	0.49	14.66	
88F00331	F	1/2	14	2.12	139.9	13.5	4.0	71.0	
88F00327	F	1/2	14	2.01	142.9	14.8	4.2	71.9	
88F00341	F	1/2	14	1.85	147.3	13.5	3.5	84.5	
88F00305	F	1/2	14	2.05	140.9	13.7	4.0	57.8	
Parameter means:				2.01	142.75	13.88	3.92	71.30	
Standard deviations:				0.11	3.28	0.62	0.30	10.91	
88F00319	F	3/2	14	2.40	144.3	14.1	3.6	77.8	
88F00304	F	3/2	14	1.74	145.7	14.3	3.2	80.1	
88F00326	F	3/2	14	2.04	146.7	14.3	3.7	41.3	
88F00312	F	3/2	14	2.16	147.1	14.6	3.9	38.7	
88F00321	F	3/2	14	2.03	145.6	14.8	4.0	38.7	
Parameter means:				2.07	145.88	14.42	3.68	55.32	
Standard deviations:				0.24	1.09	0.28	0.31	21.61	

Appendix G (cont.): SERUM CHEMISTRY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Expanded Statistical Table for COBAS II
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 17-Jan-89
Page: 4

ACUTE/ACUTE INTRAVENOUS

Animal Number	Sex	Group/ Subgroup	Day of Study	CR	ALT	TP	URIC	K	TRIG	A-G
88F00346	F	4/2	14	1.1	49.0	6.7	.1	4.8	58.	2.1
88F00351	F	4/2	14	1.1	36.2	6.7	.1	4.6	85.	3.6
88F00325	F	4/2	14	1.0	31.0	6.4	.1	3.9	33.	2.9
88F00307	F	4/2	14	1.2	58.2	6.7	.0	5.9	114.	3.2
88F00340	F	4/2	14	1.0	53.4	7.0	0	4.2	61.	3.3
Parameter means:				1.08	45.56	6.70	0.06	4.68	70.20	3.02
Standard deviations:				0.08	11.54	0.21	0.05	0.77	30.64	0.57
88F00334	F	2/2	14	1.3	28.7	6.9	.0	4.7	58.	1.7
88F00322	F	2/2	14	1.4	32.2	6.8	0	4.8	78.	2.1
88F00353	F	2/2	14	1.2	34.1	6.9	.1	4.9	102.	2.6
88F00333	F	2/2	14	1.0	29.8	6.3	.1	4.4	42.	3.0
88F00318	F	2/2	14	1.1	36.5	6.3	.0	4.4	58.	2.9
Parameter means:				1.20	32.26	6.64	0.04	4.64	67.60	2.46
Standard deviations:				0.16	3.17	0.31	0.05	0.23	23.08	0.55
88F00331	F	1/2	14	1.2	33.8	6.4	.1	3.8	49.	2.9
88F00327	F	1/2	14	1.0	27.0	6.8	.1	4.3	72.	3.3
88F00341	F	1/2	14	1.0	66.6	7.1	.1	4.5	99.	1.8
88F00305	F	1/2	14	1.4	46.4	6.4	0	4.6	79.	2.8
Parameter means:				1.15	43.45	6.68	0.08	4.30	74.75	2.70
Standard deviations:				0.19	17.40	0.34	0.05	0.36	20.63	0.64
88F00319	F	3/2	14	.8	34.0	NT	.1	6.9	205.	NT
88F00304	F	3/2	14	1.4	32.7	7.4	0	4.4	59.	1.6
88F00326	F	3/2	14	1.2	32.7	7.0	.0	4.5	42.	2.4
88F00312	F	3/2	14	1.1	25.5	7.0	.0	4.4	91.	2.8
88F00321	F	3/2	14	1.0	56.5	6.5	.0	4.8	135.	4.5
Parameter means:				1.10	36.28	6.98	0.02	5.00	106.40	2.83
Standard deviations:				0.22	11.79	0.37	0.04	1.07	65.52	1.22

Appendix H: HEMATOLOGY

List of Hematology Abbreviations/Units

RBC	Erythrocytes ($x10^6/\mu l$)
HGB	Hemoglobin (g/dl)
HCT	Hematocrit (%)
MCV	Mean Corpuscular Volume (femtoliters)
MCH	Mean Corpuscular Hemoglobin (picograms)
MCHC	Mean Corpuscular Hemoglobin Concentration (g/dl)
RET	Reticulocytes (%)
WBC	Total Leukocyte Count ($x10^3/\mu l$)
SEG	Polymorphonuclear Granulocytes (%)
BAN	Immature Neutrophils (%)
EOS	Eosinophils (%)
BAS	Basophils (%)
LYM	Lymphocytes (%)
MON	Monocytes (%)
PLT	Platelets ($x10^3/\mu l$)
NRBC	Nucleated Red Blood Cell (#/100 WBC)
PT	Prothrombin Time (Seconds)
APPT	Activated Partial Thromboplastin Time (Seconds)

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR BAKER I
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 05-Jan-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
88F00261	M	4/1	4	6.8	5.48	11.7	36.3	66.3	21.4	32.2	259.
88F00296	M	4/1	4	4.6	5.77	12.4	38.3	66.3	21.5	32.4	94.
88F00277	M	4/1	4	1.2	5.92	11.7	38.1	64.3	19.8	30.7	402.
88F00287	M	4/1	4	4.9	6.17	13.6	40.5	65.7	22.0	33.6	307.
88F00281	M	4/1	4	2.5	5.39	11.3	35.1	65.1	21.0	32.2	249.
PARAMETER MEANS:				4.00	5.75	12.14	37.66	65.54	21.14	32.22	262.20
STANDARD DEVIATIONS:				2.19	0.32	0.91	2.07	0.85	0.83	1.03	111.83
88F00274	M	2/1	4	4.2	5.24	11.1	34.3	65.4	21.2	32.4	358.
88F00258	M	2/1	4	5.6	5.64	12.4	38.6	68.5	22.0	32.1	308.
88F00285	M	2/1	4	5.3	5.77	12.6	40.4	70.0	21.8	31.2	439.
88F00260	M	2/1	4	5.5	4.96	11.4	34.8	70.2	23.0	32.8	423.
88F00293	M	2/1	4	4.9	5.55	11.3	35.8	64.5	20.4	31.6	151.
PARAMETER MEANS:				5.10	5.43	11.76	36.78	67.72	21.68	32.02	335.80
STANDARD DEVIATIONS:				0.57	0.33	0.69	2.62	2.63	0.97	0.63	115.83
88F00298	M	1/1	4	2.9	5.17	10.8	33.5	64.8	20.9	32.2	381.
88F00257	M	1/1	4	5.6	4.63	10.7	32.8	70.8	23.1	32.6	500.
PARAMETER MEANS:				4.25	4.90	10.75	33.15	67.80	22.00	32.40	440.50
STANDARD DEVIATIONS:				1.91	0.38	0.07	0.49	4.24	1.56	0.28	84.15
88F00273	M	3/1	4	5.6	6.28	11.6	40.5	64.5	18.5	28.6	558.
88F00294	M	3/1	4	2.6	5.62	12.1	37.8	67.3	21.5	32.0	1030.
88F00265	M	3/1	4	6.3	6.49	13.0	43.9	67.7	20.0	29.6	446.
88F00266	M	3/1	4	3.7	5.93	12.1	40.0	67.5	20.4	30.3	353.
88F00267	M	3/1	4	4.0	6.04	13.3	40.6	67.3	22.0	32.8	293.
PARAMETER MEANS:				4.44	6.07	12.42	40.56	66.86	20.48	30.66	536.00
STANDARD DEVIATIONS:				1.49	0.33	0.70	2.18	1.33	1.37	1.72	293.75

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR WBC DIFFERENTIAL COUNTS
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

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Page: 1

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT	RET
88F00261	M	4/1	4	40	0	0	0	54	0	6	1	NT	NT	1.9
88F00296	M	4/1	4	69	0	2	1	17	6	5	2	NT	NT	1.5
88F00277	M	4/1	4	53	0	0	5	37	1	4	1	NT	NT	5.5
88F00287	M	4/1	4	53	0	5	6	28	1	7	5	9.5	34.5	4.1
88F00281	M	4/1	4	63	0	3	0	27	3	4	8	NT	NT	4.7
PARAMETER MEANS:				55.60	0.00	2.00	2.40	32.60	2.20	5.20	3.40	9.50	34.50	3.54
STANDARD DEVIATIONS:				11.08	0.00	2.12	2.88	13.90	2.39	1.30	3.05	-	-	1.76
88F00274	M	2/1	4	32	0	2	4	54	3	5	5	NT	NT	1.5
88F00258	M	2/1	4	37	0	3	1	51	0	8	5	NT	NT	2.1
88F00285	M	2/1	4	28	0	3	4	52	2	11	8	NT	NT	1.9
88F00260	M	2/1	4	53	0	4	2	38	0	3	10	NT	NT	5.8
88F00293	M	2/1	4	59	0	2	4	29	3	3	2	NT	NT	2.1
PARAMETER MEANS:				41.80	0.00	2.80	3.00	44.80	1.60	6.00	6.00	-	-	2.68
STANDARD DEVIATIONS:				13.52	0.00	0.84	1.41	10.85	1.52	3.46	3.08	-	-	1.76
88F00298	M	1/1	4	32	0	4	0	60	3	1	4	NT	NT	1.5
88F00257	M	1/1	4	35	0	3	1	57	1	3	4	NT	NT	0
PARAMETER MEANS:				33.50	0.00	3.50	0.50	58.50	2.00	2.00	4.00	-	-	0.75
STANDARD DEVIATIONS:				2.12	0.00	0.71	0.71	2.12	1.41	1.41	0.00	-	-	1.06
88F00273	M	3/1	4	75	0	1	2	18	1	3	10	NT	NT	3.0
88F00294	M	3/1	4	9	0	0	1	85	3	4	1	NT	NT	2.6
88F00265	M	3/1	4	67	0	3	1	14	5	10	8	NT	NT	3.5
88F00266	M	3/1	4	52	0	2	8	29	0	9	8	NT	NT	4.5
88F00267	M	3/1	4	74	0	1	1	20	3	1	8	NT	NT	2.1
PARAMETER MEANS:				55.40	0.00	1.40	2.60	33.20	2.40	5.40	7.00	-	-	3.14
STANDARD DEVIATIONS:				27.52	0.00	1.14	3.05	29.47	1.95	3.91	3.46	-	-	0.92

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR BAKER I
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 05-Jan-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
88F00323	F	4/2	4	4.3	4.20	10.4	30.7	73.1	24.8	33.9	372.
88F00330	F	4/2	4	4.9	4.82	11.7	34.0	70.5	24.3	34.4	269.
88F00352	F	4/2	4	2.0	5.19	11.5	36.1	69.6	22.2	31.9	591.
PARAMETER MEANS:				3.73	4.74	11.20	33.60	71.07	23.77	33.40	410.67
STANDARD DEVIATIONS:				1.53	0.50	0.70	2.72	1.82	1.38	1.32	164.45
88F00313	F	2/2	4	2.7	5.08	11.4	33.4	65.8	22.4	34.1	48.
88F00335	F	2/2	4	6.9	3.96	9.3	28.6	72.1	23.5	32.5	252.
88F00337	F	2/2	4	4.5	4.94	11.3	34.1	69.0	22.9	33.1	324.
88F00349	F	2/2	4	1.2	4.94	11.2	34.6	70.0	22.7	32.4	325.
PARAMETER MEANS:				3.83	4.73	10.80	32.68	69.23	22.88	33.03	237.25
STANDARD DEVIATIONS:				2.45	0.52	1.00	2.76	2.62	0.46	0.78	130.71
88F00345	F	1/2	4	1.1	3.07	7.5	21.6	70.4	24.4	34.7	28.
88F00348	F	1/2	4	2.3	4.66	10.6	31.8	68.2	22.7	33.3	631.
88F00310	F	1/2	4	1.2	4.47	10.5	31.5	70.5	23.5	33.3	94.
PARAMETER MEANS:				1.53	4.07	9.53	28.30	69.70	23.53	33.77	251.00
STANDARD DEVIATIONS:				0.67	0.87	1.76	5.80	1.30	0.85	0.81	330.74
88F00311	F	3/2	4	6.4	4.89	11.6	33.6	68.7	23.7	34.5	253.
88F00314	F	3/2	4	6.5	4.55	10.3	33.0	72.6	22.6	31.2	515.
88F00347	F	3/2	4	5.5	4.43	10.4	31.2	70.4	23.5	33.3	207.
PARAMETER MEANS:				6.13	4.62	10.77	32.60	70.57	23.27	33.00	325.00
STANDARD DEVIATIONS:				0.55	0.24	0.72	1.25	1.95	0.59	1.67	166.14

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR WBC DIFFERENTIAL COUNTS
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 12-Jan-89
Page: 3

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT	RET
88F00323	F	4/2	4	44.	0.	1.	3.	46.	2.	4.	0.	NT	NT	4.7
88F00330	F	4/2	4	47.	0.	2.	3.	43.	1.	4.	0.	7.0	28.1	4.5
88F00352	F	4/2	4	31.	0.	3.	0.	63.	2.	1.	0.	NT	NT	2.7
PARAMETER MEANS:				40.67	0.00	2.00	2.00	50.67	1.67	3.00	0.00	7.00	28.10	3.97
STANDARD DEVIATIONS:				8.50	0.00	1.00	1.73	10.79	0.58	1.73	0.00	-	-	1.10
88F00313	F	2/2	4	26.	0.	0.	0.	67.	2.	5.	0.	NT	NT	3.7
88F00335	F	2/2	4	49.	0.	2.	5.	42.	2.	0.	0.	6.8	47.5	2.0
88F00337	F	2/2	4	32.	0.	0.	0.	67.	0.	1.	0.	6.5	41.1	2.0
88F00349	F	2/2	4	31.	0.	3.	2.	61.	2.	1.	0.	NT	NT	4.5
PARAMETER MEANS:				34.50	0.00	1.25	1.75	59.25	1.50	1.75	0.00	6.65	44.30	3.05
STANDARD DEVIATIONS:				10.02	0.00	1.50	2.36	11.84	1.00	2.22	0.00	0.21	4.53	1.26
88F00345	F	1/2	4	20.	0.	0.	4.	76.	0.	0.	0.	NT	NT	4.8
88F00348	F	1/2	4	54.	0.	0.	2.	41.	1.	2.	0.	NT	NT	3.4
88F00310	F	1/2	4	22.	0.	1.	0.	66.	3.	8.	0.	NT	NT	4.5
PARAMETER MEANS:				32.00	0.00	0.33	2.00	61.00	1.33	3.33	0.00	-	-	4.23
STANDARD DEVIATIONS:				19.08	0.00	0.58	2.00	18.03	1.53	4.16	0.00	-	-	0.74
88F00311	F	3/2	4	46.	0.	2.	0.	39.	2.	11.	0.	NT	NT	2.0
88F00314	F	3/2	4	49.	0.	0.	0.	48.	2.	1.	0.	NT	NT	4.0
88F00347	F	3/2	4	30.	0.	1.	3.	58.	5.	3.	0.	NT	NT	2.2
PARAMETER MEANS:				41.67	0.00	1.00	1.00	48.33	3.00	5.00	0.00	-	-	2.73
STANDARD DEVIATIONS:				10.21	0.00	1.00	1.73	9.50	1.73	5.29	0.00	-	-	1.10

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR BAKER I
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 05-Jan-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
88F00302	M	4/1	14	5.9	6.29	13.6	41.5	66.0	21.6	33.8	417.
88F00283	M	4/1	14	9.3	6.28	14.1	41.7	66.4	22.5	33.8	368.
88F00284	M	4/1	14	5.4	5.19	11.5	35.0	67.4	22.2	32.9	191.
88F00268	M	4/1	14	8.8	6.71	14.8	43.2	64.4	22.1	34.3	313.
88F00269	M	4/1	14	8.2	5.87	13.7	41.3	70.3	23.3	33.2	260.
PARAMETER MEANS:				7.52	6.07	13.54	40.54	66.90	22.34	33.60	309.80
STANDARD DEVIATIONS:				1.76	0.57	1.23	3.19	2.19	0.63	0.55	88.72
88F00295	M	2/1	14	4.2	4.27	10.2	30.2	70.7	23.9	33.8	140.
88F00289	M	2/1	14	6.4	6.40	13.3	40.3	63.0	20.8	33.0	214.
88F00290	M	2/1	14	10.0	6.17	14.0	41.4	67.1	22.7	33.8	306.
88F00279	M	2/1	14	9.1	5.33	12.4	37.1	69.6	23.3	33.4	272.
88F00263	M	2/1	14	9.3	6.09	14.0	41.7	68.4	23.0	33.6	298.
PARAMETER MEANS:				7.80	5.65	12.78	38.14	67.76	22.74	33.52	246.00
STANDARD DEVIATIONS:				2.43	0.87	1.58	4.80	2.98	1.17	0.33	69.35
88F00280	M	1/1	14	9.3	5.34	12.8	38.2	71.5	24.0	33.5	241.
88F00303	M	1/1	14	8.3	6.29	14.3	42.7	67.9	22.7	33.5	318.
88F00254	M	1/1	14	10.4	5.97	14.7	41.8	70.1	24.6	35.2	424.
88F00297	M	1/1	14	14.6	6.72	15.6	46.4	69.0	23.2	33.6	388.
PARAMETER MEANS:				10.65	6.08	14.35	42.28	69.63	23.63	33.95	342.75
STANDARD DEVIATIONS:				2.77	0.58	1.17	3.37	1.54	0.84	0.83	80.86
88F00300	M	3/1	14	8.1	6.06	13.7	41.3	68.2	22.6	33.2	321.
88F00259	M	3/1	14	7.6	5.77	13.6	40.4	70.1	23.6	33.7	195.
88F00292	M	3/1	14	7.5	6.11	13.2	39.5	64.6	21.6	33.4	293.
88F00286	M	3/1	14	7.5	6.98	14.7	44.5	63.7	21.1	33.0	409.
88F00276	M	3/1	14	11.3	5.24	12.1	36.8	70.2	23.1	32.9	395.
PARAMETER MEANS:				8.40	6.03	13.46	40.50	67.36	22.40	33.24	322.60
STANDARD DEVIATIONS:				1.64	0.63	0.94	2.80	3.05	1.04	0.32	86.41

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR WBC DIFFERENTIAL COUNTS
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 12-Jan-89
Page: 2

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT	RET
88F00302	M	4/1	14	43.	0.	4.	7.	40.	2.	4.	5.	1.7	19.5	3.9
88F00283	M	4/1	14	43.	0.	3.	0.	42.	4.	8.	0.	NT	NT	3.1
88F00284	M	4/1	14	16.	1.	1.	3.	75.	2.	2.	0.	8.0	17.7	3.9
88F00268	M	4/1	14	19.	0.	0.	2.	57.	2.	3.	4.	NT	NT	4.1
88F00269	M	4/1	14	24.	0.	1.	1.	70.	0.	4.	0.	NT	NT	4.4
PARAMETER MEANS:				29.00	0.20	1.80	2.60	56.80	2.00	4.20	1.80	4.85	18.60	3.88
STANDARD DEVIATIONS:				13.10	0.45	1.64	2.70	15.87	1.41	2.28	2.49	4.45	1.27	0.48
88F00295	M	2/1	14	11.	0.	0.	1.	87.	0.	1.	0.	NT	NT	2.6
88F00289	M	2/1	14	19.	0.	1.	2.	68.	1.	9.	0.	NT	NT	1.5
88F00290	M	2/1	14	28.	0.	5.	6.	56.	0.	4.	0.	NT	NT	1.4
88F00279	M	2/1	14	28.	0.	0.	3.	58.	4.	7.	0.	6.2	40.9	1.6
88F00263	M	2/1	14	57.	0.	3.	5.	32.	0.	3.	0.	9.5	NT	3.9
PARAMETER MEANS:				28.60	0.00	1.80	3.40	60.20	1.00	4.80	0.00	7.85	40.90	2.20
STANDARD DEVIATIONS:				17.39	0.00	2.17	2.07	19.98	1.73	3.19	0.00	2.33	-	1.07
88F00280	M	1/1	14	20.	0.	0.	3.	71.	3.	3.	0.	7.9	35.7	3.7
88F00303	M	1/1	14	25.	0.	4.	2.	62.	0.	6.	1.	NT	NT	1.9
88F00254	M	1/1	14	43.	0.	4.	2.	32.	5.	8.	0.	4.9	32.2	1.5
88F00297	M	1/1	14	65.	0.	6.	2.	14.	4.	9.	0.	2.4	1.7	2.2
PARAMETER MEANS:				38.25	0.00	3.50	2.25	44.75	3.00	6.50	0.25	5.07	23.20	2.33
STANDARD DEVIATIONS:				20.39	0.00	2.52	0.50	26.42	2.16	2.65	0.50	2.75	18.70	0.96
88F00300	M	3/1	14	20.	0.	4.	2.	71.	1.	2.	3.	6.4	15.6	4.7
88F00259	M	3/1	14	8.	0.	0.	1.	78.	5.	8.	0.	NT	NT	3.4
88F00292	M	3/1	14	45.	0.	4.	3.	45.	1.	2.	5.	7.5	18.8	2.1
88F00286	M	3/1	14	30.	0.	2.	2.	60.	2.	4.	5.	7.0	48.3	3.9
88F00276	M	3/1	14	35.	1.	1.	0.	54.	7.	2.	0.	3.3	18.7	2.2
PARAMETER MEANS:				27.60	0.20	2.20	1.60	61.60	3.20	3.60	2.60	6.05	25.35	3.26
STANDARD DEVIATIONS:				14.19	0.45	1.79	1.14	13.16	2.68	2.61	2.51	1.89	15.37	1.11

Appendix H (cont.): HEMATOLOGY

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR BAKER I
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 05-Jan-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
88F00346	F	4/2	14	6.7	5.23	11.5	34.2	65.4	22.0	33.6	432
88F00351	F	4/2	14	6.7	6.14	13.9	41.4	67.5	22.6	33.6	296
88F00325	F	4/2	14	6.1	5.37	12.1	36.6	68.2	22.5	33.1	493
88F00307	F	4/2	14	3.4	4.46	10.6	31.9	71.5	23.8	33.2	184
88F00340	F	4/2	14	8.1	6.18	13.7	41.1	66.5	22.2	33.3	560
PARAMETER MEANS:				6.20	5.48	12.36	37.04	67.82	22.62	33.36	393.00
STANDARD DEVIATIONS:				1.73	0.71	1.42	4.19	2.31	0.70	0.23	152.07
88F00334	F	2/2	14	6.1	4.62	11.0	33.3	72.1	23.8	33.0	369
88F00322	F	2/2	14	10.0	5.42	13.1	39.5	72.9	24.4	33.2	358
88F00353	F	2/2	14	6.2	5.48	12.4	36.1	65.9	22.6	34.3	259
88F00333	F	2/2	14	6.4	5.45	13.2	40.0	73.4	24.2	33.0	348
88F00318	F	2/2	14	7.7	5.09	11.4	34.0	66.8	22.4	33.5	375
PARAMETER MEANS:				7.28	5.21	12.22	36.58	70.22	23.48	33.40	341.80
STANDARD DEVIATIONS:				1.65	0.37	0.99	3.08	3.58	0.92	0.54	47.43
88F00331	F	1/2	14	6.1	5.37	12.4	37.2	69.2	23.1	33.3	255
88F00327	F	1/2	14	5.7	5.69	13.5	40.1	70.5	23.7	33.7	494
88F00341	F	1/2	14	8.0	5.44	12.9	37.8	69.4	23.7	34.1	373
88F00305	F	1/2	14	8.3	5.34	12.4	36.7	68.7	23.2	33.8	172
PARAMETER MEANS:				7.03	5.46	12.80	37.95	69.45	23.43	33.72	323.50
STANDARD DEVIATIONS:				1.31	0.16	0.52	1.50	0.76	0.32	0.33	140.43
88F00319	F	3/2	14	8.2	5.23	12.3	36.2	69.3	23.5	34.0	193
88F00304	F	3/2	14	7.5	4.43	10.1	29.7	67.1	22.8	34.0	281
88F00326	F	3/2	14	5.8	6.05	13.4	40.1	66.3	22.1	33.4	349
88F00312	F	3/2	14	2.5	3.82	8.9	25.1	65.8	23.3	35.5	159
88F00321	F	3/2	14	8.0	5.71	13.3	39.3	68.8	23.3	33.8	300
PARAMETER MEANS:				6.40	5.05	11.60	34.08	67.46	23.00	34.14	256.40
STANDARD DEVIATIONS:				2.38	0.92	2.01	6.48	1.53	0.57	0.80	78.40

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

EXPANDED STATISTICAL TABLE FOR WBC DIFFERENTIAL COUNTS
STUDY NUMBER: 88002
STUDY START DATE: 13-Sep-88

PRINTED: 12-Jan-89
Page: 4

ACUTE/ACUTE INTRAVENOUS

ANIMAL NUMBER	SEX	GROUP/ SUBGROUP	DAY OF STUDY	SEG	BAN	EOS	BAS	LYM	MON	ATL	NRBC	PT	APPT	RET
88F00346	F	4/2	14	39	0	2	2	45	0	12	0	NT	NT	3.9
88F00351	F	4/2	14	65	0	2	0	25	3	5	0	6.2	12.7	2.5
88F00325	F	4/2	14	44	0	0	1	51	0	4	0	7.1	1.4	3.5
88F00307	F	4/2	14	37	0	7	1	43	6	6	0	5.5	5.5	3.4
88F00340	F	4/2	14	20	0	2	0	29	3	4	0	5.5	16.5	3.9
PARAMETER MEANS:				41.00	0.00	2.60	0.80	38.60	2.40	6.20	0.00	6.08	9.03	3.44
STANDARD DEVIATIONS:				16.17	0.00	2.61	0.84	11.08	2.51	3.35	0.00	0.76	6.83	0.57
88F00334	F	2/2	14	10	0	0	0	11	1	1	0	8.8	14.2	4.5
88F00322	F	2/2	14	46	0	1	1	45	4	3	0	NT	NT	6.7
88F00353	F	2/2	14	39	0	0	0	58	1	2	0	NT	NT	5.1
88F00333	F	2/2	14	55	0	0	0	40	2	3	0	8.8	24.7	6.5
88F00318	F	2/2	14	51	1	0	0	47	0	1	0	NT	NT	2.4
PARAMETER MEANS:				40.20	0.20	0.20	0.20	40.20	1.60	2.00	0.00	8.80	19.45	5.04
STANDARD DEVIATIONS:				17.91	0.45	0.45	0.45	17.60	1.52	1.00	0.00	0.00	7.42	1.74
88F00331	F	1/2	14	51	0	3	0	42	1	3	0	6.0	1.2	2.9
88F00327	F	1/2	14	60	0	2	2	31	3	2	0	7.0	22.0	4.4
88F00341	F	1/2	14	54	0	2	0	39	1	4	0	NT	NT	3.1
88F00305	F	1/2	14	40	0	5	0	45	10	0	0	5.9	15.0	1.1
PARAMETER MEANS:				51.25	0.00	3.00	0.50	39.25	3.75	2.25	0.00	6.30	12.73	2.88
STANDARD DEVIATIONS:				8.38	0.00	1.41	1.00	6.02	4.27	1.71	0.00	0.61	10.58	1.36
88F00319	F	3/2	14	59	0	0	0	34	2	5	0	NT	NT	5.5
88F00304	F	3/2	14	40	0	6	0	52	0	2	0	9.5	11.5	4.3
88F00326	F	3/2	14	57	0	2	1	39	1	0	0	7.5	1.6	8.8
88F00312	F	3/2	14	33	0	5	0	52	0	10	0	NT	NT	1.3
88F00321	F	3/2	14	23	0	0	0	73	1	3	0	NT	NT	4.5
PARAMETER MEANS:				42.40	0.00	2.60	0.20	50.00	0.80	4.00	0.00	8.50	6.55	4.88
STANDARD DEVIATIONS:				15.49	0.00	2.79	0.45	15.12	0.84	3.81	0.00	1.41	7.00	2.69

Appendix I: PATHOLOGY REPORT

TOXICOLOGY STUDY NO. 88002

PRINCIPAL INVESTIGATOR: Gary M. Zaucha, DVM, CPT, VC
CO-PRINCIPAL INVESTIGATOR: Denzil F. Frost, MS, DVM, CPT, VC
PATHOLOGIST: Luann McKinney, DVM, MAJ, VC

I. INTRODUCTION

Type: Acute Rabbit Intravenous Toxicity Test
Compound: Hypertonic Saline/Dextran 70®
Animal: Oryctolagus cuniculus (New Zealand White)
Male and Female Juveniles
Dosage groups

GROUP 1	(M&F)	Hypertonic saline
GROUP 2	"	Hypertonic saline/Dextran 70®
GROUP 3	"	Dextran 70®
GROUP 4	(Control)	Lactated Ringer's Solution

Dose: 20.00 ml/kg

II. Summary of post-mortem examination procedures

Tranquilization: Ketamine and Acepromazine, IM
Clinical Lab values: Hematology and Serology
Euthanasia: Pentobarbital overdose, IV
Fixative: 10% Neutral Buffered Formalin
Histopathology: Routine light microscopy of Brain, Heart, Kidney, Liver, Lungs and Spleen.

III. GROSS FINDINGS:

PATHOLOGY TABLE 1 - Incidence Summary of all Gross Observations

Gross lesions of congestion, hemorrhage, edema, exophthalmus and blood in the nares were limited to dosing deaths in group 1 (hypertonic saline). Pitting of the renal capsule, also noted among these animals, is attributed to parenchymal swelling accentuating pre-existing interstitial lesions.

One gross lesion, disseminated hepatic foci, was observed at scheduled death; in the absence of any microscopic lesions, this mottling is attributed to post-mortem blood pooling.

Appendix I (cont.): PATHOLOGY REPORT

IV. MICROSCOPIC FINDINGS:

All specified tissues were examined in all groups.

PATHOLOGY TABLE 2 - Incidence Summary of Microscopic Observations (KOLMOGOROV-SMIRNOV 2-Tailed test, 0.05 level)
2-A - Scheduled deaths
2-B - Unscheduled deaths

PATHOLOGY ANNEX - Individual animal reports/ Gross and Microscopic

Lesions of leptomeningitis, granulomatous encephalitis, and subacute and chronic interstitial nephritis are frequently associated with infection by Encephalitozoon cuniculi, a common condition of domesticated rabbits. Lymphogranulomatous hepatitis, accompanied by some degree of biliary epithelial hyperplasia, is compatible with the recovery stage of hepatic Eimeriosis, another common condition in laboratory rabbits. The mild pulmonary inflammatory responses and splenic and pulmonary lymphoid hyperplasias are attributed to a subclinical infectious process. Glycogen storage is a physiologic change seen in animals on a high plane of nutrition.

Seen in all groups, the acute hemorrhage, congestion and edema, are attributed to hemodynamic changes associated with tranquilization and euthanasia. No microscopic lesions unique to the unscheduled deaths in group 1 were observed.

Based on the results of the Kolmogorov-Smirnov two-tailed analysis (95% confidence level) of the microscopic findings, no lesion was significantly more frequent in a treated group of either sex than in the control group. No microscopic observations are attributed to treatment effect.

Appendix I (cont.): PATHOLOGY REPORT

V. SUMMARY COMMENTS:

Lesions observed in these rabbits are considered to be either incidental lesions common to the species, or are changes associated with acute hemodynamic alterations. No morphologic evidence of toxicity of Hypertonic Saline/Dextran 70® was observed.

Luann McKinney, DVM
MAJ, VC
Diplomate, ACVP
C, Div Pathology

Appendix I (cont.): PATHOLOGY REPORT

DEFINITION OF MICROSCOPIC TERMS, BY ORGAN

I. BRAIN:

1. ENCEPHALITIS, LYMPHOGRANULOMATOUS - FOCI OF LYMPHOCYTES AND MACROPHAGES (10 TO 50 CELLS) IN THE NEUROPIL EXCLUSIVE OF PRESENCE/SEVERITY OF PARENCHYMAL DAMAGE.

2. LEPTOMENINGITIS, NONSUPURATIVE- LYMPHOCYTES AND MONONUCLEAR CELLS IN THE LEPTOMENINGES, EXTENDING TO THE VIRCHOW-ROBBINS SPACE.

II. HEART:

1. HEMORRHAGE, ACUTE, EPICARDIUM- POOLS, 25 OR MORE MICRONS IN DIAMETER,OF ERYTHROCYTES IN THE EPICARDIAL FAT AND MESENCHYME.

2. MYOCARDITIS, SUBACUTE, INTERSTITIUM- AGGREGATES OF LYMPHOCYTES, 10 OR MORE CELLS, BETWEEN MYOCARDIAL FIBERS OR IN MYOCARDIAL VASCULAR ADVENTITIA. PRESENCE/SEVERITY OF PARENCHYMAL DAMAGE NOT REQUIRED.

III. KIDNEY:

1. INFLAMMATION, SUBACUTE, PERIPELVIC FAT- AGGREGATES OF LYMPHOCYTES AND PLASMA CELLS IN THE PERIPELVIC FAT.

2. NEPHRITIS, CHRONIC, INTERSTITIUM- FOCAL INTERSTITIAL FIBROPLASIA, OFTEN WITH DEFORMATION OF NORMAL LINEAR ARRAYS OF CORTICAL ELEMENTS; USUALLY ACCOMPANIED BY LOCAL INFILTRATE OF LYMPHOCYTES/PLASMA CELLS/AND MACROPHAGES.

3. NEPHRITIS, SUBACUTE, INTERSTITIUM- AGGREGATES OF LYMPHOCYTES AND PLASMA CELLS, WITH OR WITHOUT MACROPHAGES, IN CORTICAL OR MEDULLARY INTERSTITIUM. USUALLY ACCOMPANIED BY SOME DEGREE OF DAMAGE OR DISARRAY OF THE NEPHRON.

4. VACUOLIZATION, TUBULAR EPITHELIUM- CLEAR CYTOPLASMIC VACUOLES, BOTH MULTIPLE AND SINGULAR, THAT DISPLACE THE NUCLEUS PERIPHERALLY; USUALLY SEEN AS A CLUSTER OF CROSS-SECTIONS OF ONE NEPHRON.

Appendix I (cont.): PATHOLOGY REPORT

IV. LIVER:

1. HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS- INFILTRATES OF LYMPHOCYTES, PLASMA CELLS, AND SOME MACROPHAGES AROUND BILE DUCTS AND DUCTULES, INCLUDING, BUT NOT LIMITED TO THE PORTAL TRIADS. HEPATOCYTES ARE UNAFFECTED BUT THERE ARE VARIABLE DEGREES OF BILIARY EPITHELIAL HYPERPLASIA.

2. NECROSIS, COAGULATIVE, CHRONIC- FOCI OF LOBULES OR PORTIONS OF LOBULES THAT HAVE UNDERGONE COAGULATIVE NECROSIS (CELL OUTLINES INTACT, NUCLEI NOT DISCERNABLE) AND ARE BOUNDED BY A 4-10 CELL THICK RIM OF MACROPHAGES/FIBROBLASTS.

3. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCYTES- HEPATOCELLULAR CYTOPLASM DISTENDED BY SMALL CLEAR VACUOLES; CYTOPLASM IS REDUCED TO SMALL GRANULES SUSPENDED BETWEEN THE VACUOLES; NUCLEI ARE UNAFFECTED.

V. LUNGS:

1. CONGESTION, ACUTE, VASCULATURE- VESSELS, TO INCLUDE CAPILLARIES, ARE DISTENDED BY BLOOD.

2. FREE BLOOD, AIRWAYS- BRONCHI AND/OR PRIMARY BRONCHIOLES ARE FILLED BY ERYTHROCYTES.

3. HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE- INCREASED PROMINENCE OF LYMPHOID ELEMENTS, WITH SECONDARY GERMINAL CENTER FORMATION ABOUT TERMINAL BRONCHI AND PRIMARY BRONCHIOLES.

4. INTRA-ALVEOLAR ERYTHROCYTES- APPROXIMATELY 10 OR MORE ERYTHROCYTES FREE IN THE ALVEOLAR SPACE; NO CELL RESPONSE; NO ARCHITECTURAL ALTERATION.

5. INTRA-ALVEOLAR MACROPHAGES- FOAMY OR PROTEIN-LADEN MACROPHAGES IN ALVEOLI; NUMEROUS ALVEOLI CONTAIN 3 OR MORE CELLS, OR A FOCUS OF CONTIGUOUS ALVEOLI CONTAINING 25 OR MORE.

6. INTRA-ALVEOLAR PROTEIN (EDEMA), ACUTE- ALVEOLAR SPACES FILLED WITH HOMOGENOUS PALE EOSINOPHILIC MATERIAL; NO CELLULAR RESPONSE.

Appendix I (cont.): PATHOLOGY REPORT

7. LYMPHORRHEXIS OF BRONCHIAL-ASSOCIATED LYMPHOID TISSUE- KARYORRHEXIS OF INDIVIDUAL LYMPHOCYTES OF THE 'BALT'.

8. PNEUMONIA,PYOGRANULOMATOUS,INTERSTITIUM- EXPANSION OF ALVEOLAR SEPTA AND/OR PERIBRONCHIOLAR ADVENTITIA BY VARIABLE CONCENTRATIONS OF MACROPHAGES AND EOSINOPHILIC NEUTROPHILS.

VI. SPLEEN:

1. HEMATOPOIESIS- PRESENCE OF ERYTHROID, MYELOID AND THROMBOCYTIC COLONIES IN THE RED PULP.

2. HEMOSIDEROSIS- PRESENCE OF MACROPHAGES CONTAINING VARIABLE AMOUNTS OF BROWN HEMOSIDERIN PIGMENT. USUALLY SEEN ALONG THE SINUSOIDS OF THE INTRASPLENIC TRABECULAE; SOMETIMES IN ASSOCIATION WITH ERYTHROPHAGOCYTIC MACROPHAGES.

3. LYMPHOID HYPERPLASIA- MARKED INCREASE IN WHITE PULP ELEMENTS AND RELATIVE DECREASE IN RED PULP; PRESENCE OF IMMATURE LYMPHOCYTES IN SINUSOIDS AND VASCULAR SPACES OF THE RED PULP.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Incidence Summary Report for Gross Necropsy Observations
Study Number: 88002
Report includes all dead animals
Study Start Date: 13-Sep-88

PRINTED: 23-Mar-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

	-- Males -				-- Females --			
	Ctls	1	2	3	Ctls	1	2	3
	10	10	10	10	10	10	10	10
PERITONEAL CAV.								
FRANK BLOOD PRESENT	0	0	0	0	0	2	0	0
HEMORRHAGE	0	0	0	0	0	1	0	0
EYES & OPTIC N.								
EXOPHTHALMUS	0	1	0	0	0	3	0	0
KIDNEY								
PITTED CAPSULE	0	3	0	0	0	0	0	0
LIVER								
DISSEMINATED FOCI	0	0	0	1	0	0	0	0
WHITE FOCUS,RED EDGES	0	1	0	0	0	0	0	0
CONGESTED	0	0	0	0	0	3	0	0
LUNGS								
HEMORRHAGE(S)	0	3	0	0	0	2	0	0
CONGESTION	0	0	0	0	0	3	0	0
EDEMATOUS	0	0	0	0	0	1	0	0
NOSE/TURBINATES								
BLOOD WITHIN NARES	0	1	0	0	0	1	0	0
SKIN								
HEMORRHAGE, SUBCUTANEOUS	0	0	0	0	0	2	0	0
THYMUS								
HEMORRHAGE(S)	0	3	0	0	0	0	0	0
TRACHEA								
FLUID FILLED LUMEN	0	3	0	0	0	2	0	0
WHOLE BODY								
NO GROSS LESIONS	10	7	10	9	10	7	10	10

Pathology Table 1

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Incidence Summary of Microscopic Observations
Study Number: 88002
All Diagnoses
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

Notes: Animals = all dead animals
Controls from group(s): 4

Tissues With Diagnoses	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	1	2	3	Ctls	1	2	3
	No. in group:	10	10	10	10	10	10	10	10
BRAIN .....Number examined:		10	10	10	10	10	10	10	10
LEPTOMENINGITIS, NONSUPPURATIVE		2	3	6	0	2	2	4	3
ENCEPHALITIS, LYMPHOGRANULOMATOUS		1	1	3	0	1	1	2	1
HEART .....Number examined:		10	10	10	10	10	10	10	10
HEMORRHAGE, ACUTE, EPICARDIUM		1	0	1	0	0	0	0	0
MYOCARDITIS, SUBACUTE, INTERSTITIUM		1	0	0	3	2	0	2	4
KIDNEY .....Number examined:		10	10	10	10	10	10	10	10
NEPHRITIS, CHRONIC, INTERSTITIUM		0	2	2	0	0	0	1	1
NEPHRITIS, SUBACUTE, INTERSTITIUM		2	0	4	0	1	0	3	3
INFLAMMATION, SUBACUTE, PERIPELVIC FAT		0	0	1	0	0	0	0	0
VACUOLIZATION, TUBULAR EPITHELIUM		2	0	0	0	0	1	4	1
LIVER .....Number examined:		10	10	10	10	10	10	10	10
HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS		4	3	6	2	4	3	5	4
NECROSIS, COAGULATIVE, CHRONIC		0	1	0	0	0	0	0	0
MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR		5	7	3	6	0	1	2	0
LUNGS .....Number examined:		10	10	10	10	10	10	10	10
INTRA-ALVEOLAR ERYTHROCYTES		2	6	2	3	0	2	3	3
LYMPHORRHEXIS OF BRONCHIAL-ASSOCIATED LYMPHOID TISSUE		0	2	0	0	0	0	0	0
PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM		5	3	3	2	4	0	3	3
FREE BLOOD, AIRWAYS		0	1	0	0	0	0	0	0
INTRA-ALVEOLAR MACROPHAGES		2	1	1	2	1	2	4	0
HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE		2	0	1	1	0	1	0	0
INTRA-ALVEOLAR PROTEIN (EDEMA), ACUTE		1	0	0	0	0	0	0	0
CONGESTION, ACUTE, VASCULATURE		0	0	0	0	0	1	0	0
SPLEEN .....Number examined:		10	10	10	8	10	10	10	10
HEMOSIDEROSIS		0	1	0	0	2	5	3	2
HEMATOPOIESIS		0	0	2	3	1	2	1	3
LYMPHOID HYPERPLASIA		0	0	0	0	0	1	1	1

Note: Entries flagged with a · (minus) are significantly different from control at the 0.05 level using the Kolmogorov-Smirnov two tailed test.

Pathology Table 2

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Incidence Summary of Microscopic Observations
Study Number: 88002
All Diagnoses
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

Notes: Animals = all scheduled sacrificed animal
Controls from group(s): 4

Tissues With Diagnoses		-- Animals Affected --							
	Animal sex:	-- Males --				-- Females --			
	Dosage group:	Ctls	1	2	3	Ctls	1	2	3
	No. in group:	10	7	10	10	10	7	10	10
BRAIN .....Number examined:		10	7	10	10	10	7	10	10
LEPTOMENINGITIS, NONSUPPURATIVE		2	1	6	0	2	1	4	3
ENCEPHALITIS, LYMPHOGRANULOMATOUS		1	0	3	0	1	1	2	1
HEART .....Number examined:		10	7	10	10	10	7	10	10
HEMORRHAGE, ACUTE, EPICARDIUM		1	0	1	0	0	0	0	0
MYOCARDITIS, SUBACUTE, INTERSTITIUM		1	0	0	3	2	0	2	4
KIDNEY .....Number examined:		10	7	10	10	10	7	10	10
NEPHRITIS, CHRONIC, INTERSTITIUM		0	1	2	0	0	0	1	1
NEPHRITIS, SUBACUTE, INTERSTITIUM		2	0	4	0	1	0	3	3
INFLAMMATION, SUBACUTE, PERIPELVIC FAT		0	0	1	0	0	0	0	0
VACUOLIZATION, TUBULAR EPITHELIUM		2	0	0	0	0	1	4	1
LIVER .....Number examined:		10	7	10	10	10	7	10	10
HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS		4	3	6	2	4	3	5	4
NECROSIS, COAGULATIVE, CHRONIC		0	1	0	0	0	0	0	0
MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR		5	5	3	6	0	0	2	0
LUNGS .....Number examined:		10	7	10	10	10	7	10	10
INTRA-ALVEOLAR ERYTHROCYTES		2	3	2	3	0	0	3	3
LYMPHORRHEXIS OF BRONCHIAL-ASSOCIATED LYMPHOID TISSUE		0	0	0	0	0	0	0	0
PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM		5	2	3	2	4	0	3	3
FREE BLOOD, AIRWAYS		0	1	0	0	0	0	0	0
INTRA-ALVEOLAR MACROPHAGES		2	1	1	2	1	2	4	0
HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE		2	0	1	1	0	1	0	0
INTRA-ALVEOLAR PROTEIN (EDEMA), ACUTE		1	0	0	0	0	0	0	0
CONGESTION, ACUTE, VASCULATURE		0	0	0	0	0	0	0	0
SPLEEN .....Number examined:		10	7	10	8	10	7	10	10
HEMOSIDEROSIS		0	1	0	0	2	5	3	2
HEMATOPOIESIS		0	0	2	3	1	0	1	3
LYMPHOID HYPERPLASIA		0	0	0	0	0	1	1	1

Pathology Table 2-A

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Incidence Summary of Microscopic Observations
Study Number: 88002
All Diagnoses
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 1

ACUTE/ACUTE INTRAVENOUS

Notes: Animals = unscheduled dead for study days 1- 22
Controls from group(s): 4

Tissues With Diagnoses	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	1	2	3	Ctls	1	2	3
	No. in group:	0	3	0	0	0	3	0	0
BRAIN	Number examined:	0	3	0	0	0	3	0	0
LEPTOMENINGITIS, NONSUPPURATIVE		0	2	0	0	0	1	0	0
ENCEPHALITIS, LYMPHOGRANULOMATOUS		0	1	0	0	0	0	0	0
HEART	Number examined:	0	3	0	0	0	3	0	0
HEMORRHAGE, ACUTE, EPICARDIUM		0	0	0	0	0	0	0	0
MYOCARDITIS, SUBACUTE, INTERSTITIUM		0	0	0	0	0	0	0	0
KIDNEY	Number examined:	0	3	0	0	0	3	0	0
NEPHRITIS, CHRONIC, INTERSTITIUM		0	1	0	0	0	0	0	0
NEPHRITIS, SUBACUTE, INTERSTITIUM		0	0	0	0	0	0	0	0
INFLAMMATION, SUBACUTE, PERIPELVIC FAT		0	0	0	0	0	0	0	0
VACUOLIZATION, TUBULAR EPITHELIUM		0	0	0	0	0	0	0	0
LIVER	Number examined:	0	3	0	0	0	3	0	0
HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS		0	0	0	0	0	0	0	0
NECROSIS, COAGULATIVE, CHRONIC		0	0	0	0	0	0	0	0
MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR		0	2	0	0	0	1	0	0
LUNGS	Number examined:	0	3	0	0	0	3	0	0
INTRA-ALVEOLAR ERYTHROCYTES		0	3	0	0	0	2	0	0
LYMPHORRHEXIS OF BRONCHIAL-ASSOCIATED LYMPHOID TISSUE		0	2	0	0	0	0	0	0
PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM		0	1	0	0	0	0	0	0
FREE BLOOD, AIRWAYS		0	0	0	0	0	0	0	0
INTRA-ALVEOLAR MACROPHAGES		0	0	0	0	0	0	0	0
HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE		0	0	0	0	0	0	0	0
INTRA-ALVEOLAR PROTEIN (EDEMA), ACUTE		0	0	0	0	0	0	0	0
CONGESTION, ACUTE, VASCULATURE		0	0	0	0	0	1	0	0
SPLEEN	Number examined:	0	3	0	0	0	3	0	0
HEMOSIDEROSIS		0	0	0	0	0	0	0	0
HEMATOPOIESIS		0	0	0	0	0	2	0	0
LYMPHOID HYPERPLASIA		0	0	0	0	0	0	0	0

Pathology Table 2-B

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 1
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00262 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 1 Status: FOUND DEAD Terminal body weight (kms): 3.03

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
NOSE/TURBINATES	BLOOD WITHIN NARES	
THYMUS	HEMORRHAGE(S), Trace	PETECHIAE
LUNGS	HEMORRHAGE(S), Trace	PETECHIAE
TRACHEA	FLUID FILLED LUMEN, Mild	FOAM
KIDNEY	PITTED CAPSULE, Mild	PURPLE, DIFFUSE

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Moderate, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Multifocal. LYMPHORRHEXIS OF BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 2

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00301 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.41

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Moderate, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Multifocal. FREE BLOOD, AIRWAYS, Marked, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 3

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00282 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 1 Status: FOUND DEAD Terminal body weight (kms): 3.41

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
EYES & OPTIC N.	EXOPHTHALMUS, Moderate	CLEAR CORNEA
KIDNEY	PITTED CAPSULE, Mild	PURPLE
THYMUS	HEMORRHAGE(S), Mild	PETECHIAE
LUNGS	HEMORRHAGE(S), Moderate	AND PETECHIAE
TRACHEA	FLUID FILLED LUMEN, Mild	FOAM

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Moderate, Diffuse.
KIDNEY	NEPHRITIS, CHRONIC, INTERSTITIUM, Moderate, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Multifocal. LYMPHORRHEXIS OF BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Mild, Multifocal. PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Diffuse. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Slight, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 4

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00298 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.29

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	NECROSIS, COAGULATIVE, CHRONIC, Marked, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Focal. INTRA-ALVEOLAR MACROPHAGES, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 5
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00257 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.58

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Focal. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Marked, Multifocal. PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 6

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00272 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 1 Status: FOUND DEAD Terminal body weight (kms): 3.47

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
TRACHEA	FLUID FILLED LUMEN, Mild	FOAM
THYMUS	HEMORRHAGE(S), Mild	PETECHIAE
LUNGS	HEMORRHAGE(S), Mild	AND PETECHIAE
KIDNEY	PITTED CAPSULE, Mild	PURPLE
LIVER	WHITE FOCUS,RED EDGES, Trace	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 7

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00280 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.69

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Diffuse.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Moderate, Diffuse.
KIDNEY	NEPHRITIS, CHRONIC, INTERSTITIUM, Mild, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 8
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00303 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.26

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 9
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00254 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.50

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 10

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00297 Sex: Male Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.20

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 11

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00274 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.52

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Slight, Multifocal.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Slight, Focal.
HEART	HEMORRHAGE, ACUTE, EPICARDIUM, Moderate, Focal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 12

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00258 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.32

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Focal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Diffuse.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Multifocal. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Moderate, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 13

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00285 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.19

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Focal. INTRA-ALVEOLAR MACROPHAGES, Mild, Focal. HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Mild, Focal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Multifocal. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 14
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00260 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.38

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
All protocol required tissues normal.	

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 15

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00293 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.57

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Mild, Diffuse.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Moderate, Diffuse.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Slight, Focal. INFLAMMATION, SUBACUTE, PERIPELVIC FAT, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 16

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00295 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.88

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Diffuse.
KIDNEY	NEPHRITIS, CHRONIC, INTERSTITIUM, Moderate, Multifocal. NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Focal. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Mild, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 17

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00289 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.29

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMA' ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 18

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00290 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 2.99

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 19
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00279 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.19

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse.
KIDNEY	NEPHRITIS, CHRONIC, INTERSTITIUM, Slight, Focal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 20

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00263 Sex: Male Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.53

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 21

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00273 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.05

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal. INTRA-ALVEOLAR MACROPHAGES, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 22

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00294 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.20

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Slight, Diffuse.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Diffuse. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Moderate, Diffuse.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 23

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00265 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.35

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Diffuse. PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 24

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00266 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.68

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 25
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00267 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.53

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
WHOLE BODY	NO ANIMAL TAG

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 26

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00300 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.45

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 27

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00259 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.23

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
LIVER	DISSEMINATED FOCI, Mild	MULTIPLE <1MM WHT. FOCI AT HILUS OF RT.& ACC. LIVER LOBES.

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	Required protocol tissue is missing.
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 28

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00292 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.47

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Slight, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 29

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00286 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.33

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	Required protocol tissue is missing.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 30

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00276 Sex: Male Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.45

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Mild, Diffuse.
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 31
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00261 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.35

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Multifocal.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Mild, Multifocal. HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Slight, Multifocal.
BRAIN	ENCEPHALITIS, LYMPHOGRANULOMATOUS, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 32

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00296 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.69

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 33
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00277 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.48

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
KIDNEY	VACUOLIZATION, TUBULAR EPITHELIUM, Slight, Focal.
LUNGS	HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Slight, Focal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 34

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00287 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.19

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Multifocal.
KIDNEY	VACUOLIZATION, TUBULAR EPITHELIUM, Mild, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 35
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00281 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 1 Terminal body weight (kms): 3.53

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Multifocal. PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal. INTRA-ALVEOLAR MACROPHAGES, Mild, Multifocal. INTRA-ALVEOLAR PROTEIN (EDEMA), ACUTE, Slight, Focal.
HEART	HEMORRHAGE, ACUTE, EPICARDIUM, Mild, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 36

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00302 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.27

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 37

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00283 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.56

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 38
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00284 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.12

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 39
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00268 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.36

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTER··ITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 40

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00269 Sex: Male Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.48

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Mild, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 41
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00315 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 1 Status: FOUND DEAD Terminal body weight (kms): 3.88

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
LIVER	CONGESTED, Moderate	ACUTE, DIFFUSE
LUNGS	HEMORRHAGE(S), Moderate	PETECHIAE
	CONGESTION, Moderate	DIFFUSE
PERITONEAL CAV.	FRANK BLOOD PRESENT, Mild	CLOT
	HEMORRHAGE, Moderate	RETROPERITONEAL
EYES & OPTIC N.	EXOPHTHALMUS, Moderate	CORNEA CLEAR
SKIN	HEMORRHAGE, SUBCUTANEOUS, Moderate	THORAX

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Slight, Diffuse.
LIVER	MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 42

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00339 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 1 Status: FOUND DEAD Terminal body weight (kms): 4.21

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
NOSE/TURBINATES	BLOOD WITHIN NARES, Moderate	
EYES & OPTIC N.	EXOPHTHALMUS, Moderate	CORNEA CLEAR
PERITONEAL CAV.	FRANK BLOOD PRESENT, Mild	CLOT
LUNGS	HEMORRHAGE(S), Moderate	PETECHIAE
	CONGESTION, Moderate	ACUTE
LIVER	CONGESTED, Moderate	ACUTE
TRACHEA	FLUID FILLED LUMEN, Moderate	FOAM

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 43
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00345 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 4.42

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 44

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00348 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.64

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 45
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00332 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 1 Status: FOUND DEAD Terminal body weight (kms): 4.19

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
EYES & OPTIC N.	EXOPHTHALMUS, Moderate	CORNEA CLEAR
TRACHEA	FLUID FILLED LUMEN, Moderate	FOAM
LUNGS	CONGESTION, Marked	ACUTE
	EDEMATOUS, Moderate	ACUTE
LIVER	CONGESTED, Marked	ACUTE
SKIN	HEMORRHAGE, SUBCUTANEOUS, Moderate	ECCHYMOSES

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	CONGESTION, ACUTE, VASCULATURE, Mild, Diffuse.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 46
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00310 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.74

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 47
ACUTE/ACUTE INTRAVENOUS

Animal: 88r00331 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.03

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	LYMPHOID HYPERPLASIA, Moderate.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 48

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00327 Sex: female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.98

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 49
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00341 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.88

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Diffuse.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 50

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00305 Sex: Female Group: 1 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.08

<< Gross Observations >>

Tissue	Finding, severity / Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos recorded on animal	

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Mild, Multifocal.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse.
KIDNEY	VACUOLIZATION, TUBULAR EPITHELIUM, Slight, Multifocal.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Slight, Diffuse. HYPERPLASIA, BRONCHIAL-ASSOCIATED LYMPHOID TISSUE, Mild, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Multifocal. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Moderate, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 51
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00313 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.88

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
KIDNEY	VACUOLIZATION, TUBULAR EPITHELIUM, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 52

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00308 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.75

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
KIDNEY	VACUOLIZATION, TUBULAR EPITHELIUM, Slight, Focal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 53

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00335 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.86

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Multifocal.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Multifocal. MULTIVESICULAR (GLYCOGEN) CHANGE, HEPATOCELLULAR, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 54

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00337 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.66

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Diffuse.
KIDNEY	VACUOLIZATION, TUBULAR EPITHELIUM, Mild, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002

PRINTED: 19-Apr-89
Page: 55

Study Start Date: 13-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00349 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.96

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Diffuse. HEMATOPOIESIS, Mild, Diffuse.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 56

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00334 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.11

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	LYMPHOID HYPERPLASIA, Moderate.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Focal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Diffuse. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Moderate, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 57
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00322 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.82

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Moderate, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Diffuse. PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 58

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00353 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.21

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
KIDNEY	NEPHRITIS, CHRONIC, INTERSTITIUM, Moderate, Focal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Multifocal. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Moderate, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 59
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00333 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.34

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Multifocal.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Multifocal. VACUOLIZATION, TUBULAR EPITHELIUM, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 60
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00318 Sex: Female Group: 2 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.94

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Focal. INTRA-ALVEOLAR MACROPHAGES, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 61
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00311 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.4[illegible]

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Multifocal.

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 62
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00314 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.84

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Slight, Diffuse.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Mild, Multifocal. VACUOLIZATION, TUBULAR EPITHELIUM, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Mild, Multifocal. PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Focal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 63

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00338 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.64

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	LYMPHOID HYPERPLASIA, Mild.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 64

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00344 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.98

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Slight, Diffuse.
LUNGS	INTRA-ALVEOLAR ERYTHROCYTES, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 65
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00347 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 4.13

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 66
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00319 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.09

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Mild, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 67

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00304 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.68

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
KIDNEY	NEPHRITIS, CHRONIC, INTERSTITIUM, Mild, Multifocal. NEPHRITIS, SUBACUTE, INTERSTITIUM, Moderate, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Multifocal. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Mild, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 68

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00326 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.25

<< Gross Observations >>

Tissue	Finding, severity / Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Mild, Multifocal.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 69
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00312 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.07

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP. PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 70
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00321 Sex: Female Group: 3 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.07

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
All protocol required tissues normal.	

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 71
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00323 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 4.34

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Diffuse.
KIDNEY	NEPHRITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Mild, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Mild, Diffuse. ENCEPHALITIS, LYMPHOGRANULOMATOUS, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 72

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00336 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 4.38

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
All protocol required tissues normal.	

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 73
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00330 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 4.10

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Mild, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002

PRINTED: 19-Apr-89
Page: 74

Study Start Date: 13-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00324 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice Terminal body weight (kms): 3.89

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 75

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00352 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 4 Status: Interim sacrifice 2 Terminal body weight (kms): 3.54

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
All protocol required tissues normal.	

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 76

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00346 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.50

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMOSIDEROSIS, Slight, Multifocal.
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Mild, Multifocal.
LUNGS	INTRA-ALVEOLAR MACROPHAGES, Slight, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Multifocal.
BRAIN	LEPTOMENINGITIS, NONSUPPURATIVE, Moderate, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002

PRINTED: 19-Apr-89
Page: 77

Study Start Date: 13-Sep-88

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00351 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.01

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
SPLEEN	HEMATOPOIESIS, Mild, Multifocal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 78
ACUTE/ACUTE INTRAVENOUS

Animal: 88F00325 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.09

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Multifocal.
HEART	MYOCARDITIS, SUBACUTE, INTERSTITIUM, Slight, Focal.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 79

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00307 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 4.00

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Diffuse.

Appendix I (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

Individual Animal Data Dump Table
Study Number: 88002
Study Start Date: 13-Sep-88

PRINTED: 19-Apr-89
Page: 80

ACUTE/ACUTE INTRAVENOUS

Animal: 88F00340 Sex: Female Group: 4 Dose level: 20.00 ML/KG/day
Day of death: 15 Status: Final sacrifice Terminal body weight (kms): 3.51

<< Gross Observations >>

Tissue	Finding, severity	Gross Free-Text Comments
WHOLE BODY	NO GROSS LESIONS	

<< Necropsy Memos >>

Tissue	Necropsy memos
No necropsy memos	recorded on animal

<< Pathology Observations >>

Tissue	Histopathologic diagnoses / Special histological comments
LIVER	HEPATITIS, LYMPHOGRANULOMATOUS, PORTAL TRACKS, Slight, Multifocal.
LUNGS	PNEUMONIA, PYOGRANULOMATOUS, INTERSTITIUM, Slight, Focal.

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